Sleep and Information Processing in Individuals who have Sustained a Traumatic Brain Injury

by

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Abstract

Individuals who have sustained a traumatic brain injury (TBI) often complain of trouble sleeping and daytime fatigue but little is known about the neurophysiological underpinnings of these sleep difficulties. The fragile sleep of those with a TBI was predicted to be characterized by impairments in gating, hyperarousal and a breakdown in sleep homeostatic mechanisms. To test these hypotheses, 20 individuals with a TBI (18-64 years old, 10 men) and 20 age-matched controls (18-61 years old, 9 men) took part in a comprehensive investigation of their sleep. While TBI participants were not recruited based on sleep complaint, the final sample was comprised of individuals with a variety of sleep complaints, across a range of injury severities. Rigorous screening procedures were used to reduce potential confounds (e.g., medication). Sleep and waking data were recorded with a 20-channel montage on three consecutive nights. Results showed dysregulation in sleep/wake mechanisms. The sleep of individuals with a TBI was less efficient than that of controls, as measured by sleep architecture variables. There was a clear breakdown in both spontaneous and evoked K-complexes in those with a TBI. Greater injury severities were associated with reductions in spindle density, though sleep spindles in slow wave sleep were longer for individuals with TBI than controls. Quantitative EEG revealed an impairment in sleep homeostatic mechanisms during sleep in the TBI group. As well, results showed the presence of hyperarousal based on quantitative EEG during sleep. In wakefulness, quantitative EEG showed a clear dissociation in arousal level between TBIs with complaints of insomnia and TBIs with daytime fatigue. In addition, ERPs indicated that the experience of hyperarousal in persons with a TBI was supported by neural evidence, particularly in wakefulness and

Stage 2 sleep, and especially for those with insomnia symptoms. ERPs during sleep suggested that individuals with a TBI experienced impairments in information processing and sensory gating. Whereas neuropsychological testing and subjective data confirmed predicted deficits in the waking function of those with a TBI, particularly for those with more severe injuries, there were few group differences on laboratory computer-based tasks. Finally, the use of correlation analyses confirmed distinct sleep-wake relationships for each group. In sum, the mechanisms contributing to sleep disruption in TBI are particular to this condition, and unique neurobiological mechanisms predict the experience of insomnia versus daytime fatigue following a TBI. An understanding of how sleep becomes disrupted after a TBI is important to directing future research and neurorehabilitation.

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Curriculum Studorium

Catherine Milner completed her Ph.D. in the Behavioural Neuroscience stream of the graduate program in Psychology at Brock University, under the supervision of Dr. Kimberly Cote in the Sleep Research Laboratory. Her M.A. work, carried out in the same laboratory at Brock, contributed to understanding the effects of napping on brain function and performance, in young and older adults. Her research was supported by the National Sciences and Engineering Research Council (NSERC) of Canada and the Ontario Neurotrauma Foundation (ONF). She has presented at various conferences, published journal articles on a number of topics, and received academic and travel awards.

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Meeting of the Associated Professional Sleep Societies, Chicago, IL, U.S.A., June, 2003: "Physiological Sleepiness And Performance During Continuous Sleep Restriction" – **Catherine E. Milner**, Stephanie L. Osip, Jeannette E. Moore, Brielle P. Cuthbert and Kimberly A. Cote

Canadian Psychological Association Convention, Hamilton, ON, June, 2003: "Using Q-Methodology to Investigate Health Beliefs" – **Catherine E. Milner** and Nancy DeCourville

Annual Meeting of the Society for Psychophysiological Research, Washington, D.C., U.S.A., October, 2002: "Frontal EEG Asymmetry During Sleep and Its Relation to Affective Style" – Louis A. Schmidt, Kimberly A. Cote, Diane L. Santesso and **Catherine E. Milner**

Society for Teaching and Learning in Higher Education, Hamilton, ON, April, 2002: "Some issues in creating an online student journal" – John Mitterer, Jamie Dohn, **Catherine Milner**, Claudia Megna and Leanne Gosse

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Organizational Note

This purpose of this dissertation was to provide a comprehensive investigation of the sleep of individuals with a traumatic brain injury. Thus, this document contains reviews on the following topics: sleep, event-related potentials, and traumatic brain injury. The first two chapters were intended to provide relevant background information, and to define jargon terms. This background is necessary to adequately understand the literature central to the main thesis question, and therefore was presented first.

The first chapter ("The Measurement and Regulation of Sleep") contains descriptions of how sleep and wakefulness are regulated in the sections "Homeostatic and Circadian Regulation of Sleep" and "The Neuroanatomical and Neurochemical Regulation of Sleep". Thorough reviews of quantitative measures of sleep (polysomnography, quantitative electrophysiology) follow; the methods that were employed in this thesis are described in detail. The chapter, "Event-Related Potentials in Waking and Sleep", begins with a definition of event-related potentials and a description of their measurement. Event-related potential components that are evident in wakefulness are described briefly, followed by a description of how these components change during sleep onset and in sleep. Discussion is limited to *auditory* event-related potentials because these types of paradigms were employed in the current thesis.

Finally, the third chapter of the introduction, "Traumatic Brain Injury", provides a definition of traumatic brain injury, prevalence estimates and a description of the mechanisms involved in traumatic brain injury. This section contains an overview of executive functioning impairments, slowed processing speed, and impairments in attention and working memory, functions that are typically impaired after brain injury,

and thus tested in this thesis. The last section contains a thorough review of sleep complaints following traumatic brain injury, focusing on daytime fatigue and sleepiness, disturbances in nighttime sleep (e.g., symptoms of insomnia), and changes to sleep EEG parameters following traumatic brain injury, forming the basis for the study hypotheses.

The introduction is followed by a chapter entitled "Rationale and Hypotheses" that elaborates on the rationale for the major hypotheses. The following "Method" chapter contains a description of the participants, materials, electrophysiological recording and analyses, and study procedure. It concludes with a description of the statistical data analysis approach employed in the thesis.

The results are divided into three chapters. "Sleep-Related Electrophysiology" outlines group differences in data collected during sleep, including sleep architecture, sleep phasic events, quantitative EEG, and event-related potentials. "Waking Performance, Subjective Ratings, and Electrophysiology" outlines group differences in waking data, including neuropsychological test data, behavioural data, subjective data, quantitative EEG data, and event-related potentials. "The Relationship between Sleep and Waking Function" describes correlations between sleep and waking function for the TBI and control groups. Figures and tables are embedded within these chapters.

The Results section is followed by a "Discussion" chapter, which includes a summary and interpretation of the results, in light of the hypotheses, as well as proposed future research. This summary is followed by a general discussion, which includes contributions and limitations of the study. The final written section is a general conclusion to the dissertation. References and appendices follow.

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Figure 9. Mean log transformed gamma power ($\mu V/Hz^2$) for TBIs with insomnia (light grey) and controls (black) pre-sleep on Night 1, at each of 15 electrode sites. The top row represents eyes closed sessions; the bottom row represents eyes open sessions. Left panel: low gamma (35-45 Hz) power; centre panel: mid-gamma (55-65 Hz) power; right panel: high gamma (65-75 Hz) power. Standard errors are represented by the error bars on each column. Values closer to zero represent greater power. Note that all comparisons showed that TBIs with insomnia had greater gamma power. The comparison for high gamma power with eyes closed resulted in a significant group main effect; all other comparisons resulted in significant group differences at multiple scalp sites.

Figure 10. Mean log transformed gamma power ($\mu V/Hz^2$) for TBIs with daytime fatigue (light grey) and controls (black) pre-sleep on Night 1. Group main effects are represented. The top row represents eyes closed sessions; the bottom row represents eyes open sessions. Left panel: low gamma (35-45 Hz) power; centre panel: mid-gamma (55-

65 Hz) power; right panel: high gamma (65-75 Hz) power. Standard errors are represented by the error bars on each column. Values closer to zero represent greater power. Note that all comparisons showed that TBIs with daytime fatigue had lower gamma power; comparisons for low gamma did not reach statistical significance.

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Chapter 1: The Regulation and Measurement of Sleep

The purpose of this dissertation was to investigate sleep physiology and waking function in a group of individuals with a traumatic brain injury (TBI) ranging in severity and type of sleep complaint in comparison to an age-matched group of individuals with no history of head injury who were good sleepers. Event-related potentials (ERPs) and quantitative electroencephalography (qEEG) were used as neurophysiological measures of attention and arousal in sleep/wake states. The overall aim was to investigate sleep/wake regulation and information processing in patients who have sustained a TBI. Disrupted sleep impacts the ability to learn, it affects mood, and it alters alertness throughout the day. For individuals who have sustained a TBI, some of the neurocognitive and affective sequelae they experience may, in fact, be a secondary response to disrupted sleep. In addition, for individuals with a TBI, poor sleep may impair their ability to benefit from rehabilitation and impede their overall recovery.

Sleep occurs in all mammals (Zepelin, Siegel, & Tobler, 2005). Zepelin and colleagues elaborated that the timing of sleep, preferred location for sleep, e.g., burrow, pre-sleep behaviour, and posture may all vary between species, but the reversibility of sleep and slowing of brain activity are common to all mammals. Comparisons of sleep between species have provided some information with respect to the functions of sleep. Researchers have proposed that sleep occurs for restoration, energy conservation, and/or protection from predation. Modern theories have suggested that sleep is necessary for cognitive functioning. Considering the ubiquity of sleep, it is likely that sleep serves multiple functions for both mind and body that serve to coordinate the timing and

efficiency of a variety of physiological processes, e.g., from creativity to immune response.

Homeostatic and Circadian Regulation of Sleep

In addition to understanding the functions of sleep, it is important to understand the mechanisms that contribute to the length, depth, and timing of sleep. Borbely, Baumann, Brandeis, Strauch, and Lehmann's (1981) investigation of the time-course of delta EEG power in sleep led to a theoretical model of sleep/wake regulation, often termed the "two-process model" of sleep/wake regulation. Theoretically, sleep is controlled by two independent, but interacting, processes, Process S and Process C, which reflect homeostatic and circadian mechanisms, respectively (Borbely, 1982).

The two-process model predicts levels of sleepiness and alertness, and can be used to predict performance on neurobehavioural tasks when individual sleep need is taken into account (Van Dongen, Rogers, & Dinges, 2003). The homeostatic regulation of sleep is explained by Process S, which increases exponentially as a function of prior wakefulness and decreases exponentially as a function of time asleep (Borbely, 1982). This sleep homeostasis is reflected in delta power, i.e., slow wave activity, during sleep (Borbely et al., 1981). Slow wave activity decreases exponentially as sleep progresses (Borbely, 1982) and is enhanced during recovery following sleep deprivation (Borbely, 1982; Borbely et al., 1981; Daan, Beersma, & Borbely, 1984). Thus, slow wave activity can be considered a marker of sleep pressure or depth.

This model of homeostatic regulation has been tested experimentally. For example, Knowles, Coulter, Wahnon, Reitz, and MacLean (1990) assigned participants to one of three sleep conditions: 1) 00:00 h to 03:00 h; 2) 03:00 h to 06:00 h; and, 3) 00:00 h

to 06:00 h, each following a full night of sleep. They predicted that homeostatic pressure would be greatest in the second condition because these participants would have the greatest amount of prior wakefulness. They found that these participants had a quicker sleep onset, less wakefulness during the sleep period, greater sleep efficiency, and more slow wave sleep (SWS), demonstrating that homeostatic pressure was indeed greater in the condition with the longest period of prior wakefulness. Knowles, MacLean, Salem, Vetere, and Coulter (1986) also determined that Process S accurately predicted the amount of SWS in the first hour of nocturnal sleep. Longer prior wakefulness led to exponential increases in SWS during the first hour of sleep. These results corroborated the findings of Borbely et al. (1981), who found that the percentage of SWS, but not rapid eye movement (REM) sleep, increased during recovery sleep following sleep deprivation. Dijk, Beersma, and Daan (1987) examined the relationship between delta power during sleep and prior wakefulness; they manipulated prior wakefulness by having participants take naps at different clock times (10:00 h, 12:00 h, 14:00 h, 16:00 h, 18:00 h, 20:00 h, and 04:00 h). Although sleep latency showed a circadian trend, i.e., it was shorter at the circadian nadir in alertness in the afternoon, Dijk et al. confirmed that delta power during non-REM (NREM) sleep was a function only of prior time awake, not circadian processes, i.e., it increased linearly with number of prior hours awake.

REM sleep has been shown to be controlled by circadian rhythms (Process C) instead of Process S (Dijk et al., 1987; Dinges, 1986; Taub & Berger, 1973). Dinges, for example, had participants spend 54 hours in a laboratory free of time cues. During a sleep deprivation paradigm, participants took naps at the circadian peak or trough, after various lengths of time awake. While SWS parameters depended on the length of prior

wakefulness, REM propensity was affected only by the circadian placement of the nap. More recent data indicated that REM sleep depends on homeostatic, as well as circadian, processes. Werth, Cote, Gallmann, Borbely, and Achermann (2002) selectively REM deprived participants during a daytime sleep episode that occurred after a night of sleep loss. They showed that REM propensity rose with increasing time awake, but they also showed that the rise in REM pressure was tapered by circadian processes, which predict that REM pressure will be lower in the afternoon than morning. Their data thus supported the notion that REM is controlled by Process S and Process C.

Process S interacts with Process C so that there are peaks and troughs in alertness throughout the day. Process C reflects the circadian oscillator governing the timing of sleep and wakefulness (Borbely, 1982). Circadian rhythms are controlled by the suprachiasmatic nucleus (SCN), which also regulates body temperature rhythms. Sleep propensity is thought to be highest when body temperature is at a minimum (Broughton, 1998). Following the night sleep period, humans also experience a period of peak sleepiness in mid-afternoon, at approximately 14:00 h ("afternoon nap zone"), followed by a period of heightened alertness, at approximately 20:00 h ("forbidden zone;" Broughton, 1998). Akerstedt and Folkard (1996) reported that such sleepiness in the afternoon reflects the ultradian rhythm, rather than circadian rhythm. Ultradian rhythms are biological rhythms with periods less than 24 hours (Schulz, 1993). Examples of these rhythms include NREM/REM cycles during the night and the basic rest-activity cycle during the day (Kleitman, 1967).

More recently, researchers have suggested that alertness (or sleepiness) can be predicted with a three-process model, adding Process W to the original model. Process W

is the "wakeup" process representing sleep inertia (Akerstedt & Folkard, 1994). Sleep inertia is characterized by a reduction in the ability to think and perform upon awakening due to the transition from sleep to wakefulness; confusion, grogginess, and deficits in cognitive performance may accompany this transition period (Dinges, 1993). The effects of sleep inertia typically dissipate within 30 minutes (Takahashi, 2003), but may depend on the task. Thus, Process W depends not on the amount of prior wakefulness as Process S does, but on the prior time asleep. Process W, or sleep inertia, becomes greater as the duration of the preceding sleep period lengthens. Researchers have proposed that it may not be the amount of time asleep per se that determines the level of sleep inertia, but specifically the amount of SWS obtained (Ferrara, De Gennaro, Casagrande, & Bertini, 2000). Ferrara et al. found that selective SWS deprivation made sleep lighter and therefore led to less sleep inertia upon awakening.

In sum, sleep/wake regulation is controlled by a three-process model. Homeostatic regulation is explained by Process S, which increases exponentially with prior time awake, and decreases exponentially with SWS. Circadian regulation is explained by Process C, which predicts peaks and troughs in alertness, and which interacts with Process S to predict the timing of sleep and wakefulness. Finally, Process W represents sleep inertia, and increases with prior time asleep.

The Neuroanatomical and Neurochemical Regulation of Sleep

While the three-process model of sleep/wake regulation remains a theoretical construct, neurobiological research provides information about the neuroanatomical and neurochemical factors that are involved in the regulation of sleep and wakefulness. Sleep is an active process that is controlled by specific brain regions and neurochemicals

(Jones, 2005). More precisely, the reticular activating system (RAS) of the brainstem is responsible for maintaining the waking state (Jones, 2005). Electrical stimulation of the RAS in cats has been shown to produce cortical activation, reflected in fast EEG activity (Moruzzi & Magoun, 1949). Conversely, lesions of the RAS eliminate cortical activation, replacing it with slow waves in the EEG and behavioural immobility (Lindsley, Schreiner, Knowles, & Magoun, 1950). The RAS projects to the cerebral cortex in two pathways, one through the thalamus and the other through the basal forebrain (Jones, 2005). Villablanca (1965) suggested that cortical activation can be generated by the forebrain, even following lesioning of the RAS. Coenen and Drinkenburg (2002) explained that stimulation of the RAS reduces thalamic inhibition and activates the cortex. Thus, there are multiple pathways to the cortical activation characteristic of wakefulness.

The primary neurochemicals involved in the maintenance of wakefulness are the catecholamines (dopamine and norepinephrine), acetylcholine, histamine, and glutamate (Jones, 2005). Dopamine neurons are found primarily in the substantia nigra and ventral tegmental area in the midbrain; they project to various subcortical structures to control activity in motor and limbic systems. Norepinephrine-containing neurons are located primarily in the pons and medulla; these project to both the forebrain and cerebral cortex (Nolte, 2002). Dopamine neurons are involved in behavioural arousal, while norepinephrine neurons are involved in cortical activation. Acetylcholine and histamine induce vigilance and cortical activation; however, acetylcholine is active during REM sleep as well as waking, while histamine neurons are inactive during REM (Jones, 2005). Finally, glutamate is the primary neurotransmitter of the RAS, and is therefore related to

the waking state. In fact, novel drugs manufactured to promote wakefulness, e.g., CX717 (Cortex Pharmaceuticals), act on the glutamate neurotransmitter system (Lynch & Gall, 2006).

NREM and REM sleep are controlled by brain regions that are specific to each type of sleep. Through early transection studies (e.g., Batini, Moruzzi, Palestini, Rossi, & Zanchetti, 1958) and clinical case studies (e.g., Markand & Dyken, 1976), sleep-generating structures have been identified in the lower brainstem; specifically, the pons and medulla are implicated in SWS. As well, activation of these structures inhibits activity in the RAS (Jones, 2005). Other structures involved in the generation of SWS include the nucleus of the solitary tract and the forebrain. Clinical studies of "encephalitis lethargica" suggested a sleep-promoting structure in the anterior hypothalamus and preoptic area, which was thought to balance the wakefulness-promoting posterior hypothalamus (von Economo, 1931). Finally, cortical structures (in particular, orbitofrontal regions) and the basal ganglia are important for the production of sleep (Penaloza-Rojas, Elterman, & Olmos, 1964; Villablanca & Marcus, 1972). Certain neurons in these areas are more active during SWS than during waking; however, these neurons have "burst" discharge patterns, creating the sleep spindles and delta waves that are evident in NREM sleep (Steriade, Contreras, & Amzica, 1994).

Serotonin, adenosine, and gamma-aminobutyric acid (GABA) are the primary neurochemicals that produce SWS. Not surprisingly, serotonergic neurons are located in the pons, medulla, and midbrain of the brainstem, linking them to the production of SWS (Hobson, 1995; Jones, 2005). Other research supporting this claim has shown that destruction of the serotonergic system causes a decrease in SWS (Idzikowski, 1989).

Serotonin might attenuate activation of the cortex to promote SWS (Cape & Jones, 1998); as well, serotonin neurons in the anterior hypothalamus might prepare the brain for sleep during waking hours, thereby promoting SWS (Jouvet, 1984). Adenosine promotes sleep by inhibiting neuronal firing, particularly the firing of cholinergic neurons in the brainstem and basal forebrain (Jones, 2005). Finally, GABA is the primary inhibitory neurotransmitter in the brain and promotes SWS by inhibiting the transfer of information from the thalamus to the cortex; it is also involved in the generation of sleep spindles (Jones, 2005). In fact, benzodiazepines which promote sleep act on the GABA neurotransmitter system.

Electrophysiologically, REM sleep is a very different state than SWS sleep, and is thus controlled by different neural pathways. In studying REM sleep in the cat, Jouvet (1962) identified that the brainstem was responsible for the characteristic muscle atonia and EEG firing patterns in this state. More specifically, muscle atonia occurs through inhibition of motor regions in the medulla, whereas the generation of REM EEG patterns depends on the pons (also see Siegel, 2006). In addition, the firing rate of neurons in the RAS is twice as high during both waking and REM, compared to NREM sleep (Steriade & McCarley, 1990), supporting the notion that the RAS promotes both wakefulness and REM sleep.

Neurochemically, adrenergic, serotonergic, and histaminergic cells reduce their firing during NREM sleep and more during REM; given that they are minimally active during REM sleep, they are referred to as REM-off cells (Siegel, 2006). In contrast, cholinergic agonists increase REM sleep (e.g., George, Haslett, & Jenden, 1964). Similarly, acetylcholine release is greatest during REM sleep compared to both NREM

and waking (Siegel, 2006). During REM sleep, acetylcholine is maximally released within the thalamus and cortex (Jones, 2005). Specific cholinergic neurons (REM-on cells) are maximally active during REM sleep (Siegel, 2006). Other REM-on cells may be part of the GABA or glutamate systems (Siegel, 2006).

The SCN, an area of the anterior hypothalamus, is responsible for circadian rhythms (Schwartz, 1993). Direct inputs from retinal ganglia to the SCN are necessary to regulate circadian rhythms (Schwartz, 1993). Additional light information is conveyed to the SCN indirectly through other brain regions (Schwartz, 1993). Finally, the SCN also connects to raphe nuclei and receives hormonal, i.e., melatonin, input (Schwartz, 1993). Destruction of this area in monkeys causes loss of circadian rhythms, as well as increased sleep time (Edgar, Dement, & Fuller, 1993). Conversely, electrical or pharmacological stimulation of this area in rodents results in predictable phase shifts of circadian rhythms, i.e., changes in the timing of sleep and wakefulness (Schwartz, 1993).

To summarize, early research established the RAS as the pathway that promotes and maintains wakefulness, and established that a combination of neurochemistry (dopamine, norepinephrine, acetylcholine, histamine, glutamate) is involved in the waking state. Conversely, the pons and medulla were implicated in SWS. GABA, serotonin, and adenosine neurochemically maintain this state. REM sleep is known to be generated by a combination of pontine cells and the RAS. Pontine neurons known as "REM-on" cells exert their influence through acetylcholine. Finally, the SCN is implicated in the timing of circadian rhythms. Thus, these neurobiological mechanisms underlying each sleep/wake state must be understood in order to understand the regulation of sleep and wakefulness.

Polysomnography and Sleep Architecture

In addition to an understanding of the theoretical and neurobiological mechanisms underlying sleep/wake states, an understanding of the techniques that are used to measure and analyze the depth and character of sleep is also necessary for this thesis. With the development of EEG recording technologies (Berger, 1929) and the discovery of REM sleep (Aserinsky & Kleitman, 1953), major advances in our knowledge of sleep have occurred in the past several decades. Since the 1930's, sleep has been examined using polysomnographic (PSG) recordings (Davis, Davis, Loomis, Harvey, & Hobart, 1937, 1938). These recordings have then been "scored", according to standard criteria (Rechtschaffen & Kales, 1968), by decomposing the night into 30-second epochs that are categorized as one of the five stages of sleep (Stage 1, 2, 3, 4, or REM). Advances in computer technology now allow a finer description of the depth and quality of sleep, using techniques such as power spectral analyses and period-amplitude analyses (Geering, Achermann, Eggimann, & Borbely, 1993).

Since the advent of the electroencephalogram, sleep has most typically been described by the electrophysiological characteristics of three primary measures: brain waves (EEG), eye movements (electrooculography [EOG]), and muscle activity (electromyography [EMG]). NREM and REM sleep alternate across the night (Dement & Kleitman, 1957; Rechtschaffen & Kales, 1968). Each NREM-REM cycle lasts approximately 90 minutes (Feinberg & Uchida, 1993), reflecting the basic rest-activity cycle (Kleitman, 1967).

NREM sleep is divided into four different sleep stages. According to the current standardized manual for scoring sleep in research settings (Rechtschaffen & Kales,

1968), Stage 1 is characterized by a decrease in alpha activity (8 to 12 Hz) to less than 50% of an epoch, as well as the presence of vertex sharp waves. Theta activity (4 to 8 Hz) may occur. Slow rolling eye movements and relatively high EMG are seen in Stage 1. Stage 1 is a very light stage of sleep, i.e., during Stage 1, a person may continue to respond behaviourally and physiologically to cued stimuli (Cote, 2002). It is considered a transition from wakefulness to sleep (Ogilvie, 2001). Sleep onset, the process of falling asleep, is marked by a decline in behavioural responding, increased subjective ratings of sleepiness, and changes to the EEG and other physiological measures, such as reduced heart rate and respiration (Ogilvie, 2001). Stage 2 is characterized by higher amplitude mixed-frequency EEG, phasic events such as K-complexes and sleep spindles, and the disappearance of alpha activity. The EOG and EMG contribute little to Stage 2 identification (Rechtschaffen & Kales, 1968). Stage 3 and 4 together are considered SWS, characterized by delta waves (Rechtschaffen & Kales, 1968). In healthy, young adults, delta activity comprises 20 to 50% of the epoch during Stage 3 and more than 50% during Stage 4. Again, the EOG and EMG contribute little to SWS identification (Rechtschaffen & Kales, 1968). REM sleep is characterized by mixed-frequency EEG that resembles wakefulness. It is differentiated from wakefulness by the presence of fast-frequency brain waves particular to REM sleep, i.e., sawtooth waves, as well as rapid eye movements and muscle atonia. There are alternating periods of eye movement (phasic REM) and no eye movement (tonic REM) (Rechtschaffen & Kales, 1968).

In addition to sleep macroarchitecture, reviewing sleep microarchitecture helps to provide an understanding of the brain's response to stimuli, which is one aspect of this thesis. Sleep phasic events, namely K-complexes and sleep spindles, occur in NREM

sleep. While sleep spindles have been associated with thalamocortical gating (e.g., Steriade, 2000), there is less consensus about the functional significance of the K-complex.

K-complexes. Seminal studies by Loomis and colleagues showed that the K-complex occurred spontaneously as well as in response to stimuli (Loomis, Harvey, & Hobart, 1938), varied with stage of sleep, and was maximal at frontal sites (Davis, Davis, Loomis, Harvey, & Hobart, 1939), observations that continue to hold true today. Davis et al. (1939) showed that a tone occurring two to three seconds after a K-complex was unlikely to elicit another K-complex, and Schwab, Passouant, and Cadilhac (1954) later confirmed that K-complexes occurred more frequently in response to stimuli occurring further apart, suggesting that the K-complex has a relatively long refractory period. As well, the K-complex habituates more quickly with short interstimulus intervals (Schwab et al., 1954). Finally, more frequent and larger K-complexes can be produced by more intense stimuli (Davis et al., 1939).

Later work using stimuli to evoke K-complexes made use of signal averaging techniques; these techniques were well-described by Bastien and Campbell (1992). They defined the K-complex as a negative peak that occurred between 400 and 600 ms after stimulus presentation, at least 75 μV in amplitude, and containing distinct components at particular latencies after stimulus presentation. Bastien and Campbell reported that stimulus intensity did not alter the amplitude of the evoked K-complex. A later paper by Bastien and Campbell (1994) did explain, however, that K-complex amplitude can be altered by the rate of stimulus presentation, i.e., faster rates do not allow the K-complex

to fully recover from its refractory period, which is consistent with earlier reports (e.g., Schwab et al., 1954).

With respect to its functional significance, a number of researchers have suggested that the K-complex represents an arousal response. For instance, an early paper by Beh and Barratt (1965) showed that more K-complexes were produced in response to conditioned (versus non-conditioned) stimuli, and to one's own name (versus another's name). Other investigators have studied the K-complex in relation to sleep disorders, such as periodic limb movement disorder (PLMD). For example, Montplaisir, Boucher, Gosselin, Poirier, and Lavigne (1996) showed that patients with PLMD had the same number of K-complexes as controls but had significantly more K-alpha events. While this information has been interpreted to suggest that K-complexes represent an arousal process, it seems that the presence of alpha is a better indicator of arousal.

Several other researchers have interpreted the K-complex as a sleep-protective mechanism. Halasz (1981), for example, showed that the number of K-complexes preceding slow wave sleep predicted the depth of slow wave sleep, and that the number of K-complexes increased as slow wave sleep approached. More K-complexes have been found in sleep cycles that were judged to be deeper (Halasz, Pal, & Rajna, 1985). The number of K-complexes also decreases across subsequent sleep cycles, following the same pattern as delta sleep (Halasz et al., 1985). Halasz and colleagues (1981, 1985) hypothesized that the K-complex is elicited in response to sensory input, and reflects the work of thalamic nuclei in maintaining the sleep state. Halasz (1993) studied the power spectra associated with microarousals, including K-complexes. He reported that these microarousals were associated with an elevation and then reduction in the power of most

frequency bands, such as delta and alpha, but were also associated with a prolonged dampening of sigma power, i.e., sleep spindles. He recognized that the depression of sigma activity suggests that K-complexes are associated with increased sensory processing, because the spindle is associated with thalamocortical inhibition (e.g., Steriade, 2000). However, he explained this reciprocal relationship by suggesting that K-complexes and other microarousals serve to increase arousal when needed, e.g., in response to salient stimuli, but for the most part allow the individual to remain in the sleeping state. Halasz's (2005) review maintained the same position. The most recent offering from Halasz's group (Cash et al., 2009) again argued that the K-complex represents a sleep-protective mechanism based on evidence at the neuronal level, i.e., decreased EEG power and decreased neuronal firing occur in the presence of a K-complex. Cash and colleagues also pointed out that the inhibitory nature of the K-complex has long been established in animal research.

Amzica and Steriade (1998, 2002) examined the function of the K-complex from a neurobiological perspective. They showed that K-complexes are more numerous in deep sleep, and that they become more rhythmic (at a frequency of less than 1 Hz) with deeper sleep. In their experimental work with cats, the authors (1998) showed that K-complexes could be recorded in all areas of the cortex, but were also found to reflect activity in thalamic nuclei. Amzica and Steriade (1998, 2002) proposed that the K-complex is generated by the slow oscillation (< 1 Hz) through intracortical connections in layers II-III of the cortex, and is reinforced in the thalamus by thalamocortical connections. These connections allow the K-complex to synchronize the thalamocortical network, and in turn generate other rhythmic events, such as sleep spindles and delta

waves. In line with Halasz's (1993, 2005) view of the dual roles of the K-complex in processing stimuli and maintaining the sleeping state, Amzica and Steriade (1998) confirmed that the K-complex is associated with a short burst of depolarization that reflects activation of the system, followed by a prolonged hyperpolarization, during which time no further processing can take place. To summarize, the K-complex can be considered a marker of information processing that primarily serves an inhibitory function by preserving sleep.

Sleep spindles. The sleep spindle was also described in early work by the Loomis group. Loomis, Harvey, and Hobart (1935) first described the sleep spindle as 12-15 Hz activity. However, currently two types of spindles are recognized: a lower frequency frontally-generated spindle and a higher frequency centroparietal spindle (Jobert, Poiseau, Jahnig, Schulz, & Kubicki, 1992). While the latter increases linearly through development, there is a large increase in the incidence of the former during adolescence. This differentiation suggests not only that the two spindles have different generators, but also that they serve different functions. Spindles occur in all stages of NREM sleep; however, more spindles can be found in Stage 2 sleep relative to slow wave sleep (e.g., Dijk, Hayes, & Czeisler, 1993). Consistent with this idea, sleep spindles have been found to increase across sleep cycles, as slow wave sleep decreases (e.g., Guazzelli et al., 1986).

With respect to their functional significance, experimental work with cats by Steriade (Amzica & Steriade, 2000; Steriade, 2000) has shown that sleep spindles are primarily generated by GABAergic thalamic neurons. Rhythmic firing in these neurons elicits inhibition in thalamocortical loops. This inhibition synchronizes cortical regions, promoting NREM sleep. Specifically, the slow oscillation (< 1 Hz) that appears in

NREM sleep synchronizes the firing of cortical neurons, which in turn elicits GABAergic inhibition and synchronization of thalamic neurons. This inhibition is reflected as the sleep spindle (Steriade, 2000). While generated in the thalamus, corticothalamic neurons are necessary to ensure the rhythmicity and appearance of spindles (Steriade, 2000). Work with cats (Steriade, 2000) and humans (Cote, Epps, & Campbell, 2000; Elton et al., 1997) has shown that spindles reflect the primary mechanism by which transmission of information from thalamus to cortex is inhibited.

In sum, polysomnography provides the most basic tool by which to judge depth and quality of sleep. It allows the decomposition of full-night recordings into discrete sleep stages; these stages follow typical patterns across the night and throughout the lifespan. With respect to specific features of sleep, phasic events such as K-complexes and sleep spindles are well-studied events that are easy to visually identify against background EEG. Neurobiological and electroencephalographic studies in animals and humans have suggested that K-complexes and sleep spindles reflect sleep-protective mechanisms, which inhibit further processing of non-salient information.

Quantitative Electroencephalography in Sleep

In addition to gross sleep architecture, researchers employ qEEG measurements of waking and sleep data to describe levels of alertness and to measure the quality of participants' sleep. One of the most common types of spectral analysis is the Fast Fourier Transform (FFT), which is a mathematical procedure used to decompose the EEG signal into frequency components by repeatedly measuring the area under the curve of a sinusoidal wave across the entire epoch of interest (Uchida, Feinberg, March, Atsumi, & Maloney, 1999). FFT decomposes the EEG into discrete frequency bands, e.g., delta,

theta, alpha, sigma, beta, gamma (Uchida et al., 1999). The absolute and relative amount of each type of waveform is described as "power" (μV^2 / Hz). Quantitative EEG techniques have been used to describe wakefulness, the sleep onset process, nocturnal sleep, and recovery sleep following sleep deprivation.

During wakefulness and the various stages of sleep, there are characteristic changes that take place in the EEG. During alert wakefulness, higher frequencies in the beta (15 – 25 Hz) and gamma (25 – 40 Hz) bands dominate (Makeig, Jung, & Sejnowski, 2000). These frequency ranges are thought to represent arousal and focused attention (Makeig et al., 2000). Relaxed wakefulness with the eyes closed is characterized by slower alpha activity in the 10 to 12 Hz range (Davis et al., 1937; Makeig et al., 2000). Makeig and colleagues also reported that, during drowsiness, behavioural lapses in performance, i.e., missed responses to target stimuli, were related to increases in theta (4 Hz) activity and decreases in gamma (40 Hz) activity.

Several studies have applied qEEG methods to investigate the sleep onset process. The most marked change in the EEG observed during the transition from wakefulness to sleep is the reduction in alpha power. Additionally, De Gennaro, Ferrara, Ferlazzo, and Bertini (2000) reported that increases in sigma power, which is associated predominantly with sleep spindles, corresponded to the reduction of slow rolling eye movements present in Stage 1 sleep. Increases in sigma power may signal the presence of sleep spindles and the onset of definitive sleep.

Quantitative EEG can also be used to examine the sleep EEG in full-night recordings. There are several reasons that qEEG analyses provide more information than traditional sleep stage scoring for all-night recordings (Uchida et al., 1999). First, there is

some ambiguity in scoring Stages 2, 3, and 4 based on amounts of delta waves present (Uchida et al., 1999); qEEG provides a more precise measurement of the depth of sleep based on delta power throughout these stages. Quantitative measurements of delta activity also provide information on fluctuations in sleep depth within each of these stages (Uchida et al., 1999). Second, qEEG allows analysis of the fast frequencies that are neither visible nor considered with traditional sleep stage scoring (Uchida et al., 1999).

Few studies have used qEEG techniques to describe EEG frequencies as they vary across a full night of sleep. An early report (Dumermuth et al., 1983) showed that spectral power increased with increasing depth of sleep but decreased again in REM sleep; the authors also stated that alpha power was chiefly associated with wakefulness. Armitage (1995) showed, using period amplitude analysis, that delta activity was highest in SWS and lowest in Stage 1 sleep. Theta activity was the predominant frequency in REM sleep and Stage 2 sleep. Compared to other frequencies, there was little sigma or beta power across the night. Although Armitage's study aimed to differentiate the sleep EEG of men from that of women, they found no evidence of sex differences with their measures. Studying age differences in sleep depth, Landolt and Borbely (2001) presented data for one full night of sleep for younger (mean age = 22.3 years) and older adults (mean age = 62.0 years). They reported, as expected, that older adults had lower theta, alpha, and sigma power at frontocentral sites. Differences in the theta band occurred in both NREM and REM sleep, while differences in high-alpha and low-sigma were only apparent in NREM sleep. Landolt and Borbely also reported that older adults had lower delta and high-sigma power globally. In general, qEEG data support traditional polysomnography showing that older adults have lighter, poorer sleep than younger adults.

Finally, qEEG can be used to understand recovery sleep following sleep loss, an idea that is important in understanding the homeostatic nature of sleep. Borbely (1982) noted that the amount of sleep loss experienced does not directly relate to the amount of recovery sleep obtained following sleep deprivation. He put forth the idea that it is not the amount of sleep obtained during recovery that changes, but the intensity of sleep. Borbely et al. (1981) used SWS as a marker of deep sleep, noting that SWS increases following sleep debt. The authors also found that low frequency EEG power was increased during recovery, corroborating the findings from visual scoring of delta waves. Finally, Achermann, Finelli, and Borbely (2001) reported an anterior dominance of delta activity following total sleep deprivation, which they suggested was related to a higher need for recovery in frontal areas.

In sum, qEEG techniques allow researchers to more accurately describe the depth and quality of sleep. FFT has permitted researchers to describe alertness in waking states, to predict the time-course of sleep onset, and to add to traditional sleep stage scoring for full-night recordings. FFT can help researchers to understand moment-to-moment fluctuations in sleep depth in various sleep stages, and to investigate frequencies that are not visible with traditional sleep scoring methods.

Chapter 2: Event-Related Potentials in Waking and Sleep

Definition and Measurement of Event-Related Potentials

Event-related potentials (ERPs) are electric potentials derived from brain activity recorded at the scalp (Coles & Rugg, 1995; Fabiani, Gratton, & Coles, 2000; Kutas & Dale, 1997). They are often used to measure sensory processing and higher cognitive functions, such as attention (Naatanen, 1982) and memory updating (Donchin & Coles, 1988). ERPs are time-locked to either stimulus or response (Handy, 2005), and their temporal resolution makes them ideal tools to describe the timing of various stages of information processing (Otten & Rugg, 2005).

ERP amplitude (measured in μV) is the difference in voltage between an electroencephalography (EEG) baseline occurring before the stimulus, and the peak of the wave following the stimulus (Polich & Kok, 1995). The latency of a peak (measured in ms) refers to the time from the onset of a stimulus (or response) to the point of maximum amplitude of the wave (Polich & Kok, 1995). Topographical features represent the brain regions activated by the task (Otten & Rugg, 2005).

ERP labels "P" and "N" denote the polarity of the peak (positive or negative, respectively) (Campbell, Bell, & Bastien, 1992; Hillyard & Kutas, 1983; Picton, Lins, & Scherg, 1995). Polarity depends on a number of factors, including placement of the reference electrode, baseline EEG, and the sources of the components of interest (Otten & Rugg, 2005). The "P" or "N" is then followed by a number representing its approximate latency, e.g., P50, N100, P170, N200, P300, or by a number indicating the component's ordinal position in a waveform, e.g., P1, N1, P2, N2, P3, (Campbell et al., 1992; Hillyard & Kutas, 1983; Picton et al., 1995). In the latter case, subtypes of these

components may be named, such as P3a and P3b, differentiating their topographic characteristics and functional significance (Picton et al., 1995). Some waveforms have been identified by more descriptive labels characterizing the waveform itself, e.g., slow wave, or the function of the waveform, e.g., error-related negativity (Picton et al., 1995).

Peaks and troughs in the ERP represent a composite of numerous sources of brain activity (Fabiani et al., 2000). Differential processing associated with distinct deflections is typically inferred (Donchin, Ritter, & McCallum, 1978). Donchin (1981) described "deflections" as peaks and troughs of the ERP that are functionally similar, regardless of their anatomical source. In a stricter view, Naatanen and Picton (1987) described "components" as those aspects of an ERP that have the same anatomical source in the brain. It should be noted that the term "component" is used more generally in this dissertation to refer to a peak or trough in the ERP, regardless of knowledge of the anatomical source of the deflection.

Waking Event-Related Potentials

In healthy adults, ERPs have been well-studied in the waking state. While there are numerous components that occur at short, middle, and long latencies following stimulus presentation, the following section will focus only on specific components. The mid-latency P50 component represents sensory gating when elicited with the paired-click paradigm (Adler et al., 1982; Waldo & Freedman, 1986). The oddball paradigm typically elicits long-latency components (N1, P2, P300) that represent later stimulus encoding and classification. In addition, similar components are elicited during task-specific paradigms such as the n-back working memory task (which elicits N1, P2, and P300), and the Novel P3 oddball task (which elicits both the classic P300 and a frontal, novel P3 component).

Finally, the error-related negativity (ERN) and error positivity (Pe) are response-locked components elicited in response to errors of commission in fast-paced paradigms that require a button-press response. Theses specific components are reviewed as they are pertinent to the dissertation.

Sensory gating and the P50. Sensory gating refers to the ability of the central nervous system (CNS) to inhibit irrelevant sensory input to prevent information from overloading cortical regions (Venables, 1964). Sensory gating can be measured indirectly with electrophysiological recordings of the P50 component from the primary auditory cortex and prefrontal cortex (Eccles, 1969). In the paradigm typically used to gauge sensory gating, a pair of identical auditory clicks is presented with an interstimulus interval of 500 ms and an intertrial interval of 10 s (Adler et al., 1982; Waldo & Freedman, 1986). The P50 is a positive deflection occurring 15 to 80 ms after stimulus presentation (Adler et al., 1982; Waldo & Freedman, 1986). In this so-called paired-click paradigm, healthy adults will elicit a P50 to the first click, while their response to the second click will be attenuated to about 10-20% of the first response, given that the second identical stimulus is judged as irrelevant at a sensory level (Boutros, Overall, & Zouridakis, 1991). Sensory gating is equated with P50 suppression to the second stimulus.

Information processing and long-latency components. The earliest of the long-latency components, the N1, is a negative wave peaking in amplitude 80-130 ms after stimulus onset (Schwent, Hillyard, & Galambos, 1976). It is thought to be largely exogenous (Muller-Gass & Campbell, 2002), responding to the physical properties of the

stimulus. However, it must be in some ways endogenous as well because it differs depending on an individual's level of attention (Schwent et al., 1976).

Subsequent research showed that enhanced attention does not result in an increase in N1 amplitude, per se, but rather results in the addition of a "processing negativity" (PN) wave, which overlaps in space and time with the N1 (Naatanen, 1982; see also, Hansen & Hillyard, 1983; Hillyard & Kutas, 1983; Muller-Gass & Campbell, 2002). The PN is largely endogenous; that is, it does depend on the participant's level of attention, such that when participants direct their attention to a particular stimulus, increased negativity is witnessed in the ERP to that stimulus (Muller-Gass & Campbell, 2002).

In selective attention paradigms, the PN will occur in response to both attended and unattended stimuli, with a larger amplitude occurring in response to the attended stimuli. The difference in the PN between these conditions is seen as a slow, negative wave, termed the "negative difference" wave (Nd) (Hansen & Hillyard, 1983; Hillyard & Kutas, 1983; Muller-Gass & Campbell, 2002). The onset of the Nd occurs 60-80 ms after stimulus presentation (Hillyard, 1985). The Nd provides a unique way to study attention; since the stimuli in the attended and unattended channels, e.g., left versus right ear, are the same, the Nd wave removes the exogenous effects and therefore represents only the effects of attention (Muller-Gass & Campbell, 2002).

The P2 component is a positive wave peaking 150-250 ms after stimulus onset (Crowley & Colrain, 2004; Schwent et al., 1976). The P2, like the N1, is elicited in response to both standard and rare stimuli, and is therefore at least somewhat exogenous (Crowley & Colrain, 2004; Goodin, Aminoff, & Mantle, 1986). The PN may summate with the P2 as well as with the N1, causing the P2 to appear to decrease in amplitude in

response to selective attention (Muller-Gass & Campbell, 2002). Although in most research the P2 is linked to the N1, Crowley and Colrain (2004) pointed out that the P2 can be disengaged from the N1 experimentally, developmentally, and topographically. Crowley and Colrain reported that the P2 is thought to inhibit further, irrelevant processing of non-target stimuli. Indeed, the generation of the P2 in response to non-target stimuli is most evident over frontal sites; Crowley and Colrain speculate that this effect occurs because frontal regions are involved in inhibition. In sum, the P2 is distinct from the N1, and likely represents the inhibition of irrelevant stimuli.

The P3 is commonly elicited during the "oddball paradigm". First used by Ritter and Vaughan (1969), the oddball task requires participants to detect rare tones (the "oddball" or "target") among more frequently occurring "standard" tones (see also Picton, 1992 for review). The rare tones differ by a certain characteristic, e.g., pitch, intensity, duration. The P3 is produced when the participant detects the target tone, often measured by a button-press or counting response. The P3 is largest in response to attended relative to ignored stimuli (versus "ignore" conditions) (Picton, 1992). However, the P3 is also elicited to any stimulus that is intrusive, e.g., stimuli that are loud or particularly relevant, and that therefore cannot be ignored (Putnam & Roth, 1990).

The P3 occurs approximately 300 ms after the target stimulus (thus, its other label, "P300"). The latency of the P300 will vary with the difficulty of the task, i.e., more easily discriminated targets are associated with shorter latencies. The amplitude of the P300 is approximately 10 μV (Picton, 1992), but depends on factors such as the probability of target occurrence, i.e., a larger P300 is elicited to rarer targets (Picton, 1992), and the confidence of the participant that he/she has detected the target (Hillyard,

1985). Participant factors related to level of arousal, such as food and caffeine intake, seasonal variation, i.e., amount of daylight, and fatigue also alter the P300 (Polich & Kok, 1995).

Although the P300 is essentially endogenous, Sugg and Polich (1995) showed that stimulus properties also affect the P300. These authors used tones of varying intensity (45, 60, and 75 dB) to show that as intensity increased, P300 amplitude increased and latency decreased. Subsequently, Polich, Ellerson, and Cohen (1996) confirmed these findings. For standard stimuli, lower pitched tones (250 Hz compared to 1000 Hz) yielded a smaller P300 amplitude and longer latency compared to the higher pitched tone; differences for target stimuli were not significant but followed a similar trend (Sugg & Polich, 1995). In an earlier study, Polich (1989) showed that P300 amplitude and latency were affected by the pitch of the standard and target stimuli, and that P300 latency was shorter following louder and longer target stimuli. In general, then, the P300 can be altered by both the psychological state of the participant and the physical properties of the stimuli. However, in some instances, the psychological relevance of the stimulus may be confounded by its physical properties. For instance, both loud stimuli and salient stimuli, e.g., your own name, are psychologically relevant. Thus, some stimuli may have both exogenous and endogenous properties that affect the P300.

Based on previous literature, Hansen and Hillyard (1983) remarked that the P300 may represent decision-making about further processing of the stimulus. Alternatively, the P300 may represent stimulus categorization (Kutas, McCarthy, & Donchin, 1977). Research demonstrating that the P300 can occur after a behavioural response indicates that the P300 does not represent the decision to respond (Picton, 1992) so it is important

to evaluate P300 latency in the context of reaction time. While delayed reaction times alone may indicate prolongation of motor response time, delayed reaction times accompanied by delayed P300s, or delayed P300s independent of changes to reaction time, point to delays in cognitive processing and stimulus evaluation time in particular.

Donchin and Coles (1988) have stated that the P300 represents memory updating. Specifically, this updating of working memory is needed when the infrequently occurring target stimulus is presented, so that the representation of the target is held in sensory memory. Finally, Picton (1992) has suggested that the detection of the target stimulus may reflect the conscious processing of the stimulus. In general, the latency of the P300 represents the time needed to classify a stimulus, while its amplitude represents the attention allocated to the task (Picton, 1992).

The P300 has both a parietal and frontal component, which can be differentiated. The classic P300 is maximal at central-parietal sites, it peaks at approximately 300 ms, and its amplitude varies inversely with target probability (Donchin & Coles, 1988). In contrast, an earlier "P300" (P3a) is maximal over frontal sites and peaks at approximately 250 ms (Squires, Squires, & Hillyard, 1975). In contrast to the classic P300 that is elicited when individuals attend to a target stimulus, the P3a is evoked in response to unexpected stimuli, even when individuals are not attending (Squires et al., 1975). Experimental manipulations will differentially affect the components. The frontal element is enhanced in response to complex processing relying on frontal regions, e.g., n-back working memory task, whereas the posterior P300 is diminished in the same circumstances (Segalowitz, Wintink, & Cudmore, 2001). Moreover, the frontal component diminishes, after an initial enhancement, with habituation to the stimuli or to

the task (Wintink, Segalowitz, & Cudmore, 2001). In general, the P300 is thought to be generated by multiple cortical sources (Polich & Kok, 1995).

A "novel P3" component has been recorded in response to novel environmental sounds; although it has a frontal maximum, it peaks later, i.e., at 350 ms, than the P3a (Cote, 2002; Fabiani & Friedman, 1995; Spencer, Dien, & Donchin, 1999). A number of recent studies have used environmental stimuli to investigate the properties of the novel P3. This component overlaps in time with the classic P300 (Goldstein, Spencer, & Donchin, 2002). However, its function is thought to be independent of the P300 (Goldstein et al., 2002). This idea is supported by the fact that the novel P3 and the classic P300 respond differentially to experimental manipulation (Spencer et al., 1999). Also, the novel P3 has a more frontocentral scalp distribution, while the classic P300 is maximal at parietal sites (Cycowicz & Friedman, 2004). Cycowicz and Friedman noted that the novel P3 has two different aspects, the frontal aspect that indexes novelty detection, and a posterior aspect that represents classification of the stimulus. This posterior component may also be conceptualized as a classic P300 that occurs in response to novel, non-target tones (Spencer et al., 1999). Functionally, the novel P3 may represent the automatic orienting to novel stimuli or the involuntary switching of attention (Goldstein et al., 2002). Alternatively, it may indicate the inhibition of a response when the stimulus is identified as novel (Goldstein et al., 2002).

In order to determine if it was the novelty, i.e., environmental sounds, or task relevance, i.e., being designated as a target, of the tone that led to the novel P3 being elicited, Cycowicz and Friedman (2004) hypothesized that if the novel P3 depended more on stimulus type, then environmental sounds should continue to elicit this component

even when designated as targets, while pure tones that are "novel" in a certain paradigm should not. Their results showed that the environmental sounds elicited the novel P3, regardless of whether they were designated as novels or targets. Thus, the processing of novel stimuli responds to the characteristics of the stimuli, i.e., peculiar sounds are more likely to capture attention than repetitive pure tones, and this is reflected in a positive waveform that is frontally driven.

Error-related negativity. The error-related negativity (ERN; Gehring, Goss, Coles, & Meyer, 1993), or error negativity (Ne; Falkenstein, Hohnsbein, Hoormann, & Blanke, 1990), is a response-locked negativity that occurs at frontocentral sites around the time of an erroneous response, with peak amplitude occurring approximately 50 ms after the response (Hajcak, Holroyd, Moser, & Simons, 2005). Source localization methods have identified a single generator of the ERN in the anterior cingulate cortex (Hajcak et al., 2005). The amplitude of the ERN increases when the individual is certain an error occurred (Scheffers & Coles, 2000). Moreover, trait individual differences in ERN amplitude have been shown; individuals who are more concerned about errors, such as those with obsessive-compulsive tendencies, have larger ERNs (Santesso, Segalowitz, & Schmidt, 2006). The ERN is seen following errors; thus, it was originally thought to be an index of error detection that occurred after comparing the given response to that which was required (Falkenstein et al., 1990). However, later research (Vidal, Hasbroucq, Grapperon, & Bonnet, 2000) showed that a smaller ERN occurred after correct trials. In a subsequent report, researchers hypothesized that the ERN indexed the comparison process itself, rather than its outcome (Falkenstein, Hoormann, Christ, & Hohnsbein, 2000).

The ERN is followed by a positive deflection termed the error positivity (Pe; Falkenstein et al., 1990). The Pe is usually maximal at parietal sites and peaks 200 to 400 ms after an error (Murphy, Richard, Masaki, & Segalowitz, 2006). Functionally, the Pe is thought to reflect the conscious processing of an error (Nieuwenhuis, Ridderinkhof, Blom, Band, & Kok, 2001) or an updating of the context in which the error occurred (Leuthold & Sommer, 1999), as the amplitude of the Pe is larger when errors are perceived. In general, the ERN and Pe are thought to have separate, although proximal, neural generators that result in distinct processes, namely error detection and error recognition or evaluation, respectively (Herrmann, Rommler, Ehlis, Heidrich, & Fallgatter, 2004).

Event-Related Potentials at Sleep Onset and in Sleep

The activity of the brain as indexed by ERPs has been shown to differ depending on arousal state. There are two different reasons that researchers may study ERPs in sleep. The first is to discover how brain activity and information processing differ in sleep. The second is to use sleep as a naturally-occurring change in brain state that is often characterized by properties such as reduced attention, lack of movement, and response inhibition, which for some research paradigms are particularly advantageous. For those interested in how ERPs change during sleep, there are two ways to go about studying the problem. First, many researchers have investigated how ERP components associated with waking change (or cease to exist) in sleep. Second, there are certain ERP components that are particular to sleep (therefore, often collectively termed "sleep ERPs").

Sensory gating and the P50. Previous research (e.g., Amadeo & Shagass, 1973; Bastuji, Garcia-Larrea, Bertrand, & Mauguiere, 1988; Campbell & Bartoli, 1986; de Lugt, Loewy, & Campbell, 1996; Deacon-Elliott, Bell, & Campbell, 1987; Deiber, Ibanez, Bastuji, Fischer, & Mauguiere, 1989; Harsh, Voss, Hull, Schrepfer, & Badia, 1994; Osterhammel, Shallop, & Terkildsen, 1985) has shown that short latency ERP components are unchanged in sleep, while middle latency components have been reported to respond to changes in arousal state (Campbell et al., 1992; Dieber et al., 1989).

Research examining the P50 middle latency component confirms the idea that its properties can be manipulated by arousal state. The first studies investigating the role of sleep in sensory gating with the paired-click paradigm simply examined whether a period of sleep would improve waking sensory gating. In a study by Griffith, Waldo, Adler, and Freedman (1993), a group of individuals with schizophrenia and a group of control participants completed a paired-click P50 paradigm before and after a 10-minute nap opportunity. After this small amount of sleep the P50 to test stimuli showed that suppression improved in schizophrenics at a level comparable to normal controls. Further, P50 was suppressed more in schizophrenic participants who had attained deeper sleep during the nap. Unfortunately, the P50 was not recorded during sleep in this study, so the authors could not comment on sensory gating during actual sleep.

Based on studies of rat hippocampi, Griffith et al. (1993) argued that impairments in sensory gating in schizophrenics may depend on the cholinergic system, particularly the desensitization of a particular nicotinic receptor. Given that cholinergic neurons are not active in non-rapid eye movement (NREM) sleep, this type of sleep should allow

these cells to resensitize and therefore improve sensory gating. Rapid eye movement (REM) sleep should not create improvements because cholinergic activity actually increases in this state (Griffith & Freedman, 1995). To this end, Griffith and Freedman showed that sensory gating was not improved following a period of REM sleep. Again, this study did not measure the P50 during sleep, merely before and after sleep.

In a more recent study of the P50 in sleep, Kisley, Olincy, and Freedman (2001) reported that in normal participants, sensory gating was improved during REM sleep compared to waking, i.e., P50 suppression to test stimuli was greater in REM sleep compared to waking. This result is consistent with the hypothesis that sensory gating is dependent on the cholinergic system, which is elevated in REM. The results for sensory gating during NREM sleep were inconsistent (improved for some participants, worsened for some participants, and could not be detected for others). Given that studies using slower rates of presentation identified the P50 in all stages (e.g., Kevanishvili & Von Specht, 1979; Weitzman & Kremen, 1965; Williams, Tepas, & Morlock, 1962), it is likely that measurement issues, e.g., low signal-to-noise ratio, affected the Kisley et al. (2001) study. In a similar study by the same research group, Kisley et al. (2003) reported that schizophrenics exhibited impaired gating in both waking and REM sleep. Again, the results suggested that findings are consistent between wakefulness and REM, due to cholinergic activity in both states. Results were not provided for sensory gating in NREM sleep for this group.

Long-latency components. Long-latency endogenous components are affected by arousal state, resulting in changes to their latency and amplitude during sleep. Despite these changes, researchers argue that the components in sleep parallel those in

wakefulness because they display the same responses to experimental manipulation, e.g., become attenuated with repetition, occur more quickly to salient stimuli, and they are maximal at the same scalp locations (Salisbury & Squires, 1993). Investigating ERPs throughout sleep, de Lugt et al. (1996) reported that N1 decreased in amplitude from wakefulness to slow-wave sleep (SWS); it was lowest when participants failed to behaviourally respond during the transition to sleep. As well, its latency was prolonged but its scalp distribution was preserved in sleep. The authors concluded that the change in N1 resulted from the removal of a slow negative wave, i.e., PN, at sleep onset (note that the Nd cannot exist in sleep, given that it represents the difference between attended and unattended channels, and sleepers cannot selectively attend to a particular channel).

Atienza, Cantero, and Escera (2001) summarized that the sensory and cognitive functions represented by the N1 component are active during sleep; sleepers are able to detect the presence of a stimulus and to produce an orienting response toward novel stimuli as long as the stimuli are sufficiently deviant. The N1 component has a longer latency and decreased amplitude in sleep compared to waking, indicating that these functions are slower and involve less controlled processing than in waking; this difference is especially noticeable in SWS (Atienza et al., 2001). The authors further reviewed that these changes to N1 result from inhibition of thalamocortical pathways during sleep, particularly deep sleep.

Results from Cote, de Lugt, and Campbell (2002) confirmed a smaller N1 and larger P2 in Stage 1 sleep compared to wakefulness. Moreover, these components changed systematically with progressively slower reaction times at sleep onset. Cote et al. suggested that their results might be related to inhibition of information processing as

individuals fall asleep. This study showed also that when participants responded during Stage 1, the frontal P300 component associated with stimulus processing on these trials was diminished. Thus, the authors surmised that there was a decrease in conscious processing as individuals fell asleep. Campbell and Colrain (2002) similarly stated that sleep involves gating of stimuli, resulting from a thalamocortical inhibitory loop. This loop results in less activity occurring in several cortical areas, namely the association areas and frontal lobes, compared to waking.

Work with anesthetized cats by Steriade, McCormick, and Sejnowski (1993) showed that during spindling (sleep spindles are defined as phasic, 12-16 Hz activity), the forebrain's response to external stimuli is quite attenuated; thus, Steriade and colleagues promoted the idea that spindling occurs to gate information during sleep. Elton et al. (1997) showed that the ERP was more positive on trials containing spindles, and Cote et al. (2000) reported that P2 increased in amplitude in response to loud stimuli in the presence of sleep spindles. Elton and colleagues related this increased positivity to the removal of the PN that occurs during sleep, referring to the idea that the removal of the PN reflects the inhibition of information processing. In Cote and colleagues' study, the increase in P2 was found on trials in which the spindle occurred after stimulus presentation, indicating that thalamic gating of the stimulus occurs before the scalp-recorded sleep spindle is evident (Cote et al., 2000).

Crowley and Colrain (2004) provided a detailed examination of the P2 component, in waking and sleep. They summarized that P2 is typically found to increase in amplitude at sleep onset; this amplitude continues to increase as the depth of sleep increases. More specifically, compared to wakefulness, P2 becomes larger and later in

Stage 1 sleep that still contains alpha activity, and then becomes even larger and later in Stage 1 sleep containing theta activity, reaching its maximum amplitude and latency in deep sleep. In REM sleep, the P2 component returns to approximately 50% of its waking amplitude (Campbell et al., 1992). Based on previous studies, they remarked that the augmentation of P2 in NREM sleep suggests that inhibition of information processing occurs in this state. Since P2 is largest in deep sleep, it is logical to interpret the larger P2 as representing more inhibition, since individuals are less easily aroused in SWS.

Crowley and Colrain (2004) agreed with Elton et al. (1997) that the increase in P2 may result from the removal of the PN, a phenomenon that occurs at sleep onset, when an individual fails to maintain attention. This slow, long PN summates with the long-latency components in waking, and when it is removed in sleep, other negative peaks will appear to become reduced in amplitude and positive peaks will appear to become larger. Furthermore, Campbell and Colrain (2002) have argued that the removal of PN at sleep onset may be related to frontal lobe deactivation representing decreased attention and conscious processing.

The question as to whether or not the P300 can be elicited in sleep has also been investigated. This research question is of interest because, if the P300 represents conscious processing as suggested by Picton (1992), then it would not be expected to occur in sleep. In an investigation of sleep onset using a variety of electrophysiological and behavioural measures, Ogilvie, Simons, Kuderian, MacDonald, and Rustenburg (1991) found that P300 amplitude was diminished at sleep onset. Ogilvie and colleagues presented a 5-s duration low intensity tone every 30 s. To define sleep onset, they used the latency of the response to the stimulus as an indicator of level of drowsiness; response

times were binned into four categories representing increasing levels of sleepiness, with a fifth category representing response failures. Changes to P300 were related to diminishing responsiveness to the stimulus.

Harsh et al. (1994) used an oddball task to investigate the effect of task relevance on the ERP during sleep. Participants were divided into two groups, one group that attended to stimuli during wakefulness, and another that ignored the same stimuli. Behaviourally, participants' responsiveness to the stimuli decreased through Stage 1 and Stage 2 sleep. The authors also found that the P300 became smaller and its latency longer during the transition to sleep, disappearing by Stage 2 sleep. Harsh and colleagues interpreted the delay in both reaction time and the P300 as indication of longer time required for stimulus classification.

The auditory oddball paradigm (for description, see Donchin, 1981; Picton, 1992; Sutton, Braren, Zubin, & John, 1965; Verleger, 1997) is ideal to study the P300 in sleep because the characteristics of the P300 in wakefulness are well-described, it permits study of stimulus discrimination capabilities, and auditory stimuli allow the input to be consistent even if the participant moves (Cote, 2002). Cote et al. (2002) reported that when participants detected the target stimulus, the P300 at posterior electrode sites was the same in Stage 1 sleep as in waking. At anterior sites, however, the P300 was significantly smaller in Stage 1 compared to waking. This study adds to Ogilvie and colleagues' (1991) study by investigating the topography of the P300 in sleep. In an attempt to understand their results, Cote et al. mentioned that the change in P300 at frontal sites is consistent with reports of frontal deactivation associated with cortical

slowing; they proposed that their results represented changes to frontal lobe function at sleep onset.

In addition to studying the P300 at sleep onset, it is also useful to study the P300 throughout the sleep stages. In an early study, Wesensten and Badia (1988) examined the P300 in different stages of sleep. In general, they reported a positivity that was elicited by target stimuli, i.e., high-pitched tones. Its amplitude was smaller in all sleep stages compared to the P300 in wakefulness; moreover, its latency and amplitude did not differ among sleep stages (Wesensten & Badia, 1988). The latency of this positive deflection was approximately 700 ms. Researchers now understand this component to be part of the K-complex, and it is generally labeled the P900. Given that the K-complex plays a role in information processing during sleep (Colrain, 2005), it is not surprising that Wesensten and Badia reported its response to target stimuli. In a later study, Hull and Harsh (2001) failed to identify the P300 in any stage of sleep, and instead argued that the P300 disappears in sleep and is replaced by sleep-specific positivities, i.e., P220, P450, P900.

The presence or absence of the P300 may depend on the type of stimuli used. More salient stimuli are known to capture an individual's attention more easily, even in sleep. During waking, P300 in response to one's own name will be larger with a shorter latency compared to other names (Perrin, Garcia-Larrea, Mauguiere, & Bastuji, 1999). In their study, Perrin et al. also found that a positive peak at approximately 550 ms was elicited in REM sleep in response to one's own name, but not to other names. Moreover, biologically salient stimuli, e.g., sounds that are louder, capture attention in sleep (Cote & Campbell, 1999a). Applying the same reasoning as Perrin et al., Cote and Campbell (1999a) examined the P300 in sleep using intensity deviants, rather than pitch deviants,

since a change in intensity, i.e., a louder sound, is known to be more salient and force the participant's attention (also see Cote, 2002, for a discussion of methodological problems with earlier studies). Their study revealed that in REM sleep, a P300-like positivity could be elicited. Cote and Campbell (1999a) noted that the REM-positivity was similar to the waking P300 in that it was largest to target stimuli, parietally maximal, and had a peak latency of 321 ms. The authors noted that for the REM-P300 to be elicited, target stimuli must be both loud and rare. In addition to this REM-P300, Cote and Campbell (1999a) also discovered that a frontal P3a component was elicited in REM; this P3a waveform indicates that at least pre-conscious processing of the stimulus takes place in REM sleep (Cote & Campbell, 1999a). Finally, Cote, Etienne, and Campbell (2001) detected a positivity in Stage 2 sleep peaking at approximately 450 ms; citing their own and other researchers' previous work on the P300 in sleep (Cote & Campbell, 1999a; Winter, Kok, Kenemans, & Elton, 1995), they argued that this wave was not a true P300 due to its delayed latency, the fact that it was maximum over occipital sites, and the fact that it did not vary with manipulations of stimulus probability. Positivities occurring in this latency range are more likely to be components of elicited K-complexes, rather than the P300 (Cote, 2002). For example, the P450 appears to be a sleep-related ERP component that is evoked in NREM sleep to both frequent and rare stimuli.

Cote and Campbell (1999a) used stimuli that were both rare and intense, and therefore the elicitation of the P300 could not be solely related to one property (Cote & Campbell, 1999b). Therefore, in a subsequent study, Cote and Campbell (1999b) investigated the role of stimulus intensity by using tones of 0, 60, 80, and 100 dB, while holding the probability of the stimulus constant. They reported that only the loudest tones

elicited a P300 in REM sleep, but that this P300 was still attenuated from waking and only occurred parietally. This result confirmed that biologically salient stimuli capture attention in sleep. Thus, both psychologically and biologically salient stimuli are processed in REM sleep, and this processing is reflected as the P300 component.

N350 and the vertex sharp wave. While falling asleep, many ERP components seen in waking disappear, and are replaced by components specific to sleep. Winter et al. (1995) showed that sleep onset is characterized by elements of both waking, e.g., presence of N1, and sleep, e.g., presence of P200, N350, or P450. Voss and Harsh (1998) reported that the P300 (elicited to one's own name during waking) seemed to be replaced by the N350 component at sleep onset. Voss and Harsh suggested that while the P300 indexes a person's attention being directed toward a stimulus, the N350 may indicate that sensory processing is being blocked or CNS activation is being attenuated, presumably to promote sleep. Harsh (1994) reiterated that the P300 reflects orienting, and the N350 reflects inhibition.

Moreover, Kallai, Harsh, and Voss (2003) suggested that the amplitude of the N350 begins to increase at sleep onset in an effort to overcome the 40 Hz response to sensory stimulation that is associated with attention in waking, and which reappears in REM (Llinas & Ribary, 1993). As N350 increases while an individual falls asleep, this 40 Hz response disappears (Kallai et al., 2003). These results further suggest that the N350 reflects a sleep-promoting mechanism.

Harsh et al. (1994) described that the N350 was largest at the vertex and occurred in both attend and ignore conditions, to both target and non-target stimuli. Colrain, Webster, Hirst, and Campbell (2000) agreed that the N350 will be produced in response

to both rare and frequent tones and that it does not seem to vary with stimulus probability. Furthermore, although the N350 occurred in response to targets and non-targets, the amplitudes of the P220, N350, and P450 components were larger to target stimuli, indicating that the transition to sleep continues to be marked by the ability to differentiate between stimulus categories (Harsh et al., 1994). Bastien, Crowley, and Colrain (2002) reviewed that the N350 itself is also larger to target than non-target stimuli.

The morphology of the N350 resembles the vertex sharp wave that is seen in the background of the EEG in Stage 1 sleep (Harsh et al., 1994). Colrain et al. (2000) have also argued that the N350 is related to the vertex sharp wave, an EEG signature in the theta range observed in late Stage 1 sleep. The N350 (labeled "N300" in Colrain and colleagues' study) was largest in trials in which the vertex sharp wave was visually identified (Colrain et al., 2000), demonstrating the connection between the N350 component and the vertex sharp wave. Additionally, Bastien et al. (2002) reviewed that the N350 component is largest in averages containing the vertex sharp wave for both auditory and respiratory stimuli. With respect to its functional significance, Bastien et al.'s summary that the N350 is sensitive to stimulus category suggests that the related vertex sharp wave reflects an alerting process, that is, a mechanism to alert the sleeper to the salience of the target stimulus. However, given that the vertex sharp wave occurs during the transition to sleep and it exists in the theta range, an argument could be made that it is a sleep-promoting process.

N550 and the K-complex. K-complexes are phasic events that occur only in NREM sleep; although they occur in SWS, they are difficult to identify by eye against the

large amplitude background EEG, and are thus most visible in Stage 2 sleep. They may be evoked by external stimuli (Loomis et al., 1938) or they may be elicited spontaneously (Davis et al., 1939; Loomis et al., 1938). The N550 in averaged ERPs is generally thought to be the large negative peak visible in the K-complex (Bastien & Campbell, 1992). Research showing that the N350 is larger on trials in which a K-complex is produced (Bastien & Campbell, 1992) suggests that the K-complex, or N550, may in fact be triggered by the N350. Similarly, another study showed that on K-complex trials, the N350, P450, N550, and P900 were all elicited, while only the N350 was produced on trials without K-complexes (Niiyama, Fushimi, Sekine, & Hishikawa, 1995). Sallinen, Kaartinen, and Lyytinen (1997) hypothesized that the N350 may be a precursor to the K-complex because 1) N350 amplitude to deviant stimuli was larger on trials where the N350 was followed by a K-complex (see also Colrain et al., 2000), and 2) K-complexes were always preceded by the N350.

Earlier research established that the K-complex can be elicited either in response to external stimuli (Loomis et al., 1938) or elicited spontaneously (Davis et al., 1939; Loomis et al., 1938). Roth, Shaw, and Green (1956) originally described the K-complex as an "all-or-none" phenomenon, claiming that its amplitude did not vary with stimulus parameters. One problem with this research is that the K-complex cannot be measured reliably because the background EEG is so large in NREM sleep. Thus, Campbell, Bell, and Deacon-Elliott (1985) later attempted to use stimulus averaging techniques to reduce the background EEG, i.e., it should average to a zero baseline; however, this research was problematic because the authors failed to distinguish between trials on which K-complexes were elicited and those on which they were not. Thus, Bastien and Campbell

(1992) binned their data according to the presence or absence of K-complexes. They reported that the probability of eliciting a K-complex with a standard stimulus (80 dB with a 2 ms rise-fall time) was 0.50. The probability decreased with less intense (quieter) stimuli and longer rise-fall times, but did not vary by pitch. Its amplitude and latency did not vary with stimulus parameters, confirming that it is an "all-or-none" phenomenon.

Harsh and others (1994) showed that the N550 and P900 in sleep were well defined for target stimuli to which participants previously attended while awake, compared to other standards and target stimuli that were ignored when participants were awake. Another study showed that the K-complex was elicited more often in response to a rare stimulus than to the frequent stimulus (Niiyama et al., 1995). Colrain, Webster, and Hirst (1999) added that the K-complex can be elicited by both external, e.g., auditory tones, or internal, e.g., brief respiratory occlusions, stimuli and that the probability that a K-complex will occur varies with the intensity of the stimulus. Colrain and colleagues confirmed that the N550 is larger to rare than frequent stimuli, and larger when participants were asked to detect targets when they were awake compared to when no instructions were provided. These results do not contradict the idea that the K-complex is an all-or-none phenomenon because they merely show that the K-complex is responsive to relevant, target stimuli. Finally, the N550 is dependent more on rarity than on task relevance; this feature may suggest that this component contains an element of novelty detection or orienting. Moreover, the K-complex is maximal frontally when investigated with different stimulus modalities (Colrain et al., 1999; Cote, de Lugt, Langley, & Campbell, 1999). Presently, a controversy over whether the K-complex serves an arousal or sleep-promoting function remains (Wauquier, Aloe, & Declerck, 1995).

Last, the N350 and N550, as well as the P900, may depend on homeostatic mechanisms. Peszka and Harsh (2002) investigated ERPs in two 20-min naps, separated by 20 min, at bedtime immediately before a night of sleep deprivation and in another two 20-min naps at bedtime on the following night. They hypothesized that if sleep ERP components reflected information processing and arousal, they would be attenuated following sleep loss, but if they reflected sleep-promoting mechanisms, they would be enhanced following sleep deprivation (reflecting increased homeostatic sleep pressure). The authors examined sleep ERP components and visually scored phasic events during sleep onset. Given that the naps were only 20 min in length, no data were available with regard to SWS. In general, the findings revealed that N350, N550 and P900 all increased in amplitude following sleep deprivation throughout all of the sleep onset period. As well, visually identified vertex sharp waves and K-complexes increased in number following deprivation, while stimulus-evoked arousals decreased (Peszka & Harsh, 2002). These results support the idea that K-complexes reflect sleep-promoting phasic events.

Sleep positivities. In a preliminary investigation of the positivities that are specific to sleep, Harsh et al. (1994) reported that the P300 disappeared by Stage 2 sleep. In sleep, the P450 as well as both the P220 and P900 were present, and were all sensitive to stimulus probability. The authors noted that the P450, which appears in sleep, resembles the waking P300, but may be more related to the frontally generated P3a component. Compared to the P300, the sleep positivities represent different scalp topographies and latencies, and are therefore hypothesized to have different functions than the waking P300 (Hull & Harsh, 2001). More specifically, in her review of the P300

in sleep, Cote (2002) summarized that a small, positive wave with a latency of approximately 400 to 450 ms can be elicited in Stage 2 sleep after a rare, deviant stimulus. Cote remarked that that this NREM P450 is different from the waking P300 because it has a longer latency, while Hull and Harsh (2001) stated that its reduced amplitude distinguished it from the P300. As well, Cote argued that the NREM P450 has a different scalp topography from the P300, suggesting that the two components are generated by different processes. Finally, the NREM P450 does not vary by probability, differentiating it from the classic waking P300 (Cote, 2002).

In a systematic investigation of these components, Hull and Harsh (2001) manipulated stimulus probability and task relevance, which are known to affect the waking P300, in order to assess the effect of these variables on the sleep components. In concordance with previous results, they found a P300 only during wakefulness. In sleep, the P220, P450 and P900 were elicited as expected. The P220 and P900 to target stimuli were largest when target stimuli had the lowest probability of being delivered (20%). For both components, the opposite was found for non-target stimuli. Finally, these sleep ERP components were absent or obscured in REM sleep (Hull & Harsh, 2001). In general, there are a number of components that have been shown experimentally to be specific to sleep, and which have been differentiated from components that occur in wakefulness at similar latencies.

Chapter 3: Traumatic Brain Injury

Traumatic Brain Injury Definition and Classification

Traumatic brain injury (TBI) refers to sudden injury to the brain that often results from a motor vehicle collision, fall, assault, or sports injury. The American Congress of Rehabilitation Medicine's (ACRM; 1993) definition of mild TBI includes any period of loss of consciousness (LOC), loss of memory for events immediately before or after the injury, alteration in mental state at the time of the injury, and/or focal neurological deficit(s). Specifically, mild TBI is limited to situations in which post-traumatic amnesia (PTA) is not greater than 24 hours, Glasgow Coma Scale (GCS; Teasdale & Jennett, 1974) scores are 13 to 15 (where GCS scores can range from 3 to 15, with 15 being the highest level of functioning) after 30 minutes, and LOC is 30 minutes or less. Injuries exceeding these limits may be described as moderate or severe TBIs. The ACRM definition does not necessitate the head being struck and does not require that evidence of trauma be visible on neuroimaging scans. Williamson, Scott, and Adams (1996) described that mild TBIs are characterized by LOC of less than 20 minutes and PTA lasting for less than 24 hours; moderate TBIs are characterized by LOC lasting 20 minutes to 36 hours with PTA lasting one to seven days; severe TBIs involve LOC longer than 36 hours and PTA longer than seven days. Finally, concussion refers to immediate effects created by disturbance in neuronal functioning related to acceleration/deceleration injuries (Lezak, Howieson, & Loring, 2004). Concussion is often thought of as a transient disruption in the functioning of the brain and that it is reversible (Swenson, 1997).

In describing continuing problems following injury, the World Health Organization (WHO; 1978) defined post-concussive syndrome (PCS) as the presence of

three or more symptoms persisting for more than three months following a head injury. Swenson (1997) and Bernstein (1999) summarized that PCS consists of physical, e.g., headache, cognitive, e.g., impaired concentration, behavioural, e.g., poor social functioning, and affective or psychiatric symptoms, e.g., irritability. Swenson also indicated that different symptoms follow different time courses, with some appearing much later, i.e., several weeks after the injury, than others.

Researchers must consider a variety of these definitions when deciding on participant inclusion/exclusion criteria. Often, researchers focus on individuals who have sustained mild TBIs. One typical example of research criteria is provided by Bazarian et al. (1999); they included patients who had suffered a blow to the head, had a loss of consciousness of not more than 10 minutes or had amnesia for the event, had a GCS rating of 15 on emergency room presentation, had no skull fracture or focal injury, were not admitted to hospital for reasons related to head injury, and had no pathology according to a Computerized Tomography (CT) scan. The authors also included several exclusion criteria, such as alcohol and drug use, and use of medications affecting cognitive functioning, such as benzodiazepines and antidepressants. Bernstein (1999) provided similar research criteria, listing a GCS rating of 13 to 15, absence of skull fracture or focal injury, normal neurological examination, LOC for less than 30 minutes, and PTA lasting less than 24 hours.

Epidemiology of Traumatic Brain Injury

TBI is a widespread problem that affects its sufferers in numerous ways. Bazarian and colleagues (1999) reported that the most common source of minor head injury was motor vehicle collisions, followed by falls, and then sports. More women incurred injury

from motor vehicle collisions, while more men incurred injury from sports. Bazarian et al. (2005) reported that falls were the more frequent mechanism of mild TBI for the very old and the very young, while middle age groups incurred mild TBIs most often from motor vehicle collisions and assaults. Children and adolescents often received mild TBIs from both bicycle accidents and sports. Abelson-Mitchell (2008) reviewed studies of TBI incidence from 1990 to 2005, and found that younger men and older adults were most susceptible to sustaining a TBI. Younger men were most likely to accrue a TBI in a motor vehicle collision or work accident, or through physical violence. Older people were most likely to accrue a TBI as a pedestrian in a motor vehicle collision and through falls. TBI was more common in lower socioeconomic groups (Abelson-Mitchell, 2008).

Bazarian and colleagues (2005) pooled U.S. emergency room visits between the years 1998 and 2000, and reported that 878 of these visits were related to mild TBI. Based on these data, they estimated that the national incidence of mild TBI in the United States was 503.1 mild TBIs per 100 000 emergency room visits per year. In this same report, they provided prevalence estimates by a number of demographic variables: mild TBI occurred most prevalently in men, American Indians and Alaskan Natives, those under five years of age, those living in the Midwest, and those living in non-urban areas.

In a Canadian study of the incidence of TBI, Wong, Dornan, Schentag, Ip, and Keating (1993) examined admissions to a hospital-based TBI rehabilitation program between the years 1978 and 1991. The authors reported that patients had a mean age of 38.3 years, with most injuries occurring between the ages of 21 and 30. More than three times as many men than women were admitted. Average patient education level matched that of the general Canadian public. With respect to their injuries, the majority of injuries

were caused by motor vehicle collisions (43.1%) or falls (32.7%). Only 6.7% of patients reported a previous brain injury. Female patients were more likely to be older and better educated than male patients. Moreover, women were less likely to have an alcohol-related injury and more likely to have a motor vehicle-related injury, although they were also more likely to be passengers than drivers. Finally, women who sustained a TBI due to a fall were more likely to have fallen due to increasing age, while men were more likely to have fallen due to alcohol.

Several researchers have also examined the incidence of cognitive sequelae resulting from the brain injury. Bazarian and others (1999) reported that the incidence of PCS among individuals with "minor" head injuries was 58% one month after their injury, 43% three months post-injury, and 25% six months post-injury. However, it should be noted that 34% of orthopedic controls, i.e., those sustaining broken bones but not head trauma as a result of the accident, met the criteria for PCS one month post-injury. In concordance with these findings, other researchers reported that of 100 individuals who had experienced a mild head injury, 62% reported at least one symptom three months post-injury, while the mean number of symptoms reported was slightly greater than three (Ingebrigtsen, Waterloo, Marup-Jensen, Attner, & Romner, 1998). Forty percent of participants, in fact, reported at least three symptoms (thereby meeting the diagnosis for PCS). The report of symptoms did not differ by factors such as age or gender.

Mechanism of Injury

Mechanisms of injury such as motor vehicle collisions, falls, sports, and assaults have a number of characteristics in common that make the ensuing brain injuries similar in both the way that the injury occurs and the resulting impairment. Lezak et al. (2004)

described that, in these types of injuries, the energy involved in the event, e.g., force of energy in a fall, causes acceleration/deceleration of the brain, and this forward and back movement is usually accompanied by a rotational component. Damage to neurons in the region of impact (coup) and those in areas on the opposing side of the brain (contrecoup) are caused by the brain's contact with bony protrusions on the inside of the skull (Levin & Kraus, 1994). It should be noted that this type of injury can occur in the absence of direct impact to the head (Lezak et al., 2004). Movement of the brain also causes damage to axons in the cerebrum and brainstem (Lezak et al., 2004). This white matter shearing is referred to as diffuse axonal injury, and is often complicated by hemorrhaging (Mamelak, 2000). The severity of injury is dictated by factors such as velocity, duration, and direction of movement (Halliday, 1999).

Damage is likely to occur in orbitofrontal, ventral frontal, dorsolateral frontal, and anterior temporal brain regions. These regions are particularly vulnerable due to both the increased frequency of impact to the front of the head, and to greater force being exerted on these areas due to the shape and composition, i.e., bony protrusions, of the inside of the skull (Levin & Kraus, 1994; Mamelak, 2000). Axonal shearing and damage to the brain stem are also prevalent (Levin & Kraus, 1994; Potter, Jory, Bassett, Barrett, & Mychalkiw, 2002). Finally, secondary effects, such as swelling to the brain, fever, and infection, can complicate the effects of the primary injury (Lezak et al., 2004).

Giza and Hovda (2001) explained that a sudden neurotransmitter release occurs with traumatic injury to the brain, initiating a neurometabolic cascade. Using electroencephalography to study TBI, Shaw (2002) concluded that cortical activity following TBI was excitatory, i.e., epileptiform. More specifically, glutamate binds to N-

methyl-D-asparate (NMDA) receptors, resulting in excess neuronal depolarization (Giza, Griesbach, & Hovda, 2005). At the same time that glutamate depolarizes the brain, potassium is released into the extracellular space and exceeds the amount that can be taken up by nearby glia (Giza & Hovda, 2001; Giza et al., 2005). This massive potassium efflux further promotes neuronal depolarization; this excitation is followed by a depressive state that may be responsible for early loss of consciousness, amnesia, and cognitive impairment (Giza & Hovda, 2001). Giza (Giza & Hovda, 2001; Giza et al., 2005) provided a detailed description of the energy crisis experienced by the nervous system at the time of injury. The sodium-potassium pump works hard to maintain the potential of the neuron, thus requiring extra energy under these circumstances. In response to this energy requirement, the nervous system rapidly uses available cerebral glucose. This rapid utilization of energy is followed by a neuronal depression and reduced cerebral blood flow. At this point, the system fails to receive energy typically obtained through glucose and oxygen delivered by the blood; therefore, the system meets its energy requirements though increased glycolysis, which produces lactate and results in neuronal dysfunction. In addition, there is a build-up of intracellular calcium, which impairs cellular metabolism and worsens the cerebral energy crisis. Other researchers have added that changes to calcium levels also impair neuronal mitochondria, thereby altering the ability of the cell to utilize energy (Sullivan, Rabchevsky, Waldmeier, & Springer, 2005); therefore, increases in calcium may also promote cell death. These physiological changes often result in acute behavioural and cognitive changes, which potentially become long-term impairments (Sullivan et al., 2005).

Other physiological consequences of brain injury cause further complications. Such consequences include ischemia (reduced blood supply), edema (swelling), and inflammation representing infection (Wieloch & Nikolich, 2006). In particular, edema, or swelling of the brain, causes reduced delivery of glucose and oxygen to neurons, and therefore contributes to additional tissue loss (Unterberg, Stover, Kress, & Kienin, 2004). Edema can result from changes to cellular ions; when there is an increase in the number of water-binding ions in the cell, swelling occurs. Edema may also result from disruptions in the integrity of the blood-brain barrier (Unterberg et al., 2004). Intracellular swelling also further utilizes energy and contributes to the cerebral energy crisis (Unterberg et al., 2004).

Neuropsychological and Electrophysiological Indices of Impairment Following TBI

TBI is characterized by difficulties in numerous domains of functioning, including sensorial and motor systems, verbal and visual processing, attention, learning and memory, executive functioning, and social/emotional functioning (Lezak et al., 2004). For this dissertation, a focused approach was taken to investigate waking function in participants with TBI. Specifically, tasks were chosen to sample several domains of functioning, i.e., executive functioning, information processing speed, and attention/working memory, that were expected to be related to sleep impairments. The following review of the literature will focus on these specific domains of functioning.

Executive functioning. Executive functions refer to higher-order cognitions that allow individuals to engage meaningfully in goal-directed behaviours (Bamdad, Ryan, & Warden, 2003). These functions include awareness, initiation, planning, organization, and goal setting (Bamdad et al., 2003), as well as working memory, problem-solving, and set

shifting (Demakis, 2004). Executive functions are subserved by the frontal lobes and depend on communication between cortical and subcortical regions; thus, lesions in either cortical or subcortical structures can impair executive functioning (Bamdad et al., 2003). Impaired executive functioning can have widespread effects, including impaired attention, poor response inhibition, and distractibility (Busch, McBride, Curtiss, & Vanderploeg, 2005). Bamdad and others illustrated that specific effects are related to specific types of damage to the frontal lobes. For instance, damage to the dorsolateral prefrontal cortex will result in the dysexecutive syndrome characterized by a reduced ability to integrate sensory information, as well as a tendency toward inflexible or perseverative responding and poorer error monitoring. Damage to orbitofrontal regions will result in disinhibition, impulsivity, and socially inappropriate behaviour. Finally, damage to medial frontal regions will result in apathy, diminished responsiveness, and difficulty initiating behaviour (Bamdad et al., 2003).

Kim and colleagues (2005) recently looked at one particular aspect of executive function, the ability to direct and control attention. They reasoned that this aspect of attention most closely mimics real-world attention (or the necessity to direct attention in a less structured environment than that which occurs in a laboratory or neuropsychology clinic). Results supported their hypotheses, showing that executive function impairments lead to problems of inattentiveness, over and above that which was related to either age or level of disability. Moreover, slowed information processing did not account for this relationship (Kim et al., 2005).

Another specific aspect of executive functioning is the ability to inhibit a response when certain rules or contexts no longer apply. Often, individuals who have experienced

a traumatic brain injury will have difficulty inhibiting a prepotent response or ongoing action, or have difficulty using contextual cues to select the appropriate response. Potter et al. (2002) reported that a TBI group responded as quickly on a computer-based version of the Stroop Test as controls, but made more errors, consistent with their limited ability to inhibit prepotent responses. However, Seignourel et al. (2005) recently remarked that researchers examining this type of inhibition have reported mixed results. Moreover, using the Stroop, these authors attributed so-called inhibition difficulties to deficits in cognitive control, specifically what they termed context maintenance (defined as the use of information held in mind in order to dictate behaviour suitable to the task; Seignourel et al., 2005). Seignourel and colleagues agreed that impairments in inhibition result from damage to the prefrontal cortex, and results from McDonald et al. (2005) support the idea that inhibitory control is subserved by the frontal lobes, particularly the left frontal lobe. Moreover, when performing cognitively challenging tasks, functional magnetic resonance imaging (fMRI) results have suggested that individuals with TBI require the activation of larger cerebral networks than non-injured individuals (Scheibel et al., 2003). This finding indicates that more effort is needed for these individuals to perform the same task as controls.

Novelty detection is also frequently interrupted after TBI. Rugg and colleagues (1993) used a three-stimulus oddball event-related potential (ERP) task to study novelty detection in individuals who had sustained a severe closed head injury. Results showed that, for the patient group, N2 to target stimuli was larger, P3b, i.e., P300 to target stimuli, was smaller, and the novel P3 was smaller; in general, the authors noted that ERPs became more negative from 200 ms post-stimulus onward. The authors suggested

that participants with a TBI needed to recruit additional attentional resources to perform the task. In a more recent study, Segalowitz, Bernstein, and Lawson (2001) used a variety of auditory ERP tasks and found, in general, that the amplitudes of the novel P3 component and the P3b component were reduced, suggesting that individuals with mild head injury had reduced attentional ability or attentional control. Behaviourally, the patient group performed as well as controls, i.e., at ceiling, on two easy oddball tasks, but when task difficulty was increased, the patient group had longer reaction times and lower accuracy than controls; these results confirmed the authors' expectations that patients with mild head injury would show impairments on complex attention tasks.

Solbakk, Reinvang, and Andersson (2002) used a three-stimulus ERP paradigm, in which participants were to respond to target tones that were shorter in duration than more frequently-occurring standard tones. Also present were bursts of white noise that served as distractor stimuli. Solbakk and colleagues reported that individuals with brain injuries had longer reaction times to target stimuli that were accompanied by delays in P300 latency, compared to healthy controls. In addition, the amplitudes of both P3b to the target stimuli and P3a to the distractors were reduced compared to those of controls. In contrast to their hypotheses, the authors suggested that the patient group was less able to appropriately allocate attentional resources to deviant stimuli. Similarly, Daffner et al. (2000) asked participants to view visual stimuli. Participants controlled the duration of time they viewed each stimulus by pressing a button to view the next stimulus. The authors reported that patients with frontal lobe injuries spent shorter amounts of time attending to novel stimuli compared to non-injured controls. Furthermore, over time, individuals with frontal lobe injuries spent less and less time viewing such stimuli, while

controls did not show such a trend. The authors attributed these findings to the apathy that can be descriptive of frontally-injured individuals, and moreover implicated the dorsolateral prefrontal cortex in these effects. It is possible that individuals with frontal lobe injuries were less able to maintain their attention for the entire duration of the task.

Information processing speed. Slowed information processing speed is one outcome of diffuse axonal injury, the tearing and shearing of long conduction fibres (Mathias, Beall, & Bigler, 2004); injury prohibits these long fibres from transmitting information at the same rate as pre-injury. As such, cognitive efficiency is reduced; individuals with less efficient cognitive systems have to maintain effortful processing for a greater length of time (Potter et al., 2002). As evidence of this, Felmingham, Baguley, and Green (2004) reported that participants with diffuse axonal injury had slower information processing than individuals with focal traumatic brain injuries.

Mathias, Beall et al. (2004) used visual and tactile reaction time tasks to study how speed of processing is affected following TBI. Mathias, Bigler et al. (2004) argued that reaction time tasks are more sensitive to subtle disruptions in information processing caused by impaired inter-hemispheric processing following damage to white matter tracts. Mathias, Beall et al. showed that individuals who had sustained TBIs were slower and less accurate than controls on tasks that measured ability to switch attention, ability to select relevant information, design fluency (or constructional abilities), verbal learning, and recall of verbal information. More specifically, the TBI participants were slower on more difficult tasks, i.e., tasks that required incompatible responses, and therefore relied on inter-hemispheric responding. Mathias, Bigler et al. later explained these findings as resulting from damage to white matter pathways, particularly the corpus callosum.

Using an ERP paradigm, Lew, Lee, Pan, and Date (2004) showed that individuals with TBI had smaller P300 amplitudes along with longer P300 latencies to target stimuli. Lew and colleagues suggested that individuals with TBI had difficulty organizing and categorizing the stimuli. These ERP differences were accompanied by delays in behavioural reaction time, suggesting that both cognitive and motoric slowing occurred. In contrast, Fong, Chan, Ng, and Ng (2009) used a variety of measures to evaluate both motor and cognitive speed in outpatients with TBI. While slowing was found on measures of simple reaction time and cognitive processing speed, there were no differences between outpatients with TBI and those without on measures of dexterity or motor speed.

An interesting study was designed to investigate the speed-accuracy tradeoff in individuals with a TBI and controls (Battistone, Woltz, & Clark, 2008). Participants completed a visual scanning task, during which they scanned an array of number stimuli for a target (Battistone et al., 2008). On some trials, participants could be flexible about when they responded, while on other trials, there was a fixed time at which they responded. In the former condition, those with a TBI were slower but no less accurate than controls (Battistone et al., 2008). For the latter condition, the timing of the response varied. The authors thus examined at which response time participants could achieve accuracy in responding. They reported that controls could achieve accuracy at an earlier time than participants with a TBI (Battistone et al., 2008). These results supported both the idea that brain injury reduces individuals' capacity for speeded responding but also increases their cautiousness in responding. This research suggests that processing speed

deficits are complex and multi-factorial, and more research needs to be conducted to determine the sources of slowed processing speed.

Finally, ERPs can be used to estimate improvements in information processing speed, and thereby can be used to measure recovery from TBI. Keren, Beu-Dror, Stern, Goldberg, and Groswasser (1998) demonstrated that P300 latency was more prolonged in severely injured individuals compared to those less severely injured. The authors also recognized that ERP latencies (N2, P300) shortened during recovery from head injury; this effect paralleled recovery on neuropsychological measures. Gaetz, Goodman, and Weinberg (2000) consistently showed that individuals who had sustained three or more concussions had longer P300 latencies; the authors linked this finding to reported symptoms such as memory problems and cognitive slowing.

Attention/working memory. Finally, brain injury often results in impairments in various facets of the attentional system. One aspect of the attentional system is the ability to perform two tasks at the same time. This dual-tasking relies on both the ability to divide one's attention and the capacity of the working memory system. McDowell, Whyte, and D'Esposito (1997, 1998) noted that the dorsolateral prefrontal cortex is critical to the integrity of this system. One study comparing acute (less than 30 days after injury) and non-acute (more than 30 days after injury) closed head injuries showed that only those who had recently sustained a head injury displayed difficulties with dual-tasking (Vilkki, Virtanen, Surma-Aho, & Servo, 1996). However, McDowell et al. (1997) showed response slowing in a more general group of individuals with a TBI, and explained that the greater increase in response slowing during a dual-task condition indicated that poorer TBI performance is not due to lower arousal level or general

slowing. The authors also commented that dual-tasking is an appropriate measure of "real world" abilities. Other studies also showed that dual-tasking is impaired following TBI. Leclerq et al. (2000) showed that, following brain damage, reaction times on two different tasks were longer when the tasks were performed simultaneously. Thus, individuals with TBI performed each task more slowly than controls, but also had an increase in reaction time during a dual-task condition that was disproportionately larger than the increase seen for controls. The same research group (Azouvi et al., 2004) later replicated these findings. Chan's (2002) study of individuals with post-concussive complaints showed deficits in attention over and above any deficits related to emotional disturbance or processing speed.

The n-back working memory task is a complex task that places heavy demand on attentional resources. In a study by Asloun et al. (2008), 43 patients with severe TBIs completed an n-back task with three difficulty levels. Participants also completed a choice visual reaction time task. To examine the process of dual-tasking, participants also completed both tasks simultaneously, i.e., they responded to targets defined by both tasks. Not surprisingly, impairments were greatest for the highest difficulty level, and for the dual-tasking condition. However, there was no interaction between difficulty level and single- or dual-tasking.

Interestingly, Newsome et al. (2007) used fMRI to examine differences in brain activation between individuals with a severe TBI and orthopedic controls while they performed an n-back working memory task using face stimuli. The participants completed the task under low and high difficulty conditions. Under the low difficulty condition, controls activated bilateral frontal regions more extensively than individuals

with a TBI, but those with a TBI activated posterior regions more so than controls. However, there were no differences evident under the high difficulty condition (Newsome et al., 2007). The authors recognized that working memory load might decrease over time, as participants became familiar with stimuli that were repeated throughout the tasks. Therefore, they also examined changes in brain activation over time in each group. Descriptively, they reported that controls had decreases in activation in frontal and posterior regions during the low difficulty condition, while participants with a TBI had increases in those and other regions during the same condition. During the high difficulty condition, both groups showed decreases in fusiform and parahippocampal gyri, but only controls had increases in activation in frontal, temporal, and parietal regions (Newsome et al., 2007). In general, these results show that there are underlying differences in the recruitment of brain regions to support attention and working memory in individuals with a severe TBI.

Selective attention can be defined as the ability to focus on certain information while limiting distraction from other, irrelevant information (Simpson & Schmitter-Edgecombe, 2000). Solbakk, Reinvang, Nielsen, and Sundet (1999) used ERPs to examine the degree to which task-irrelevant stimuli distracted individuals with mild closed head injuries. The researchers employed a dichotic listening task, in which participants were to detect a target tone, among more frequently-occurring non-target stimuli, in one ear, while ignoring all stimuli in the other ear. Behaviourally, individuals with head injuries were distracted by the frequently-occurring irrelevant stimuli. This inability to inhibit the processing of these stimuli was represented electrophysiologically by smaller P2 ERP components compared to normal controls (Solbakk et al., 1999).

Selective attention depends, in part, on how well individuals can attend to relevant information and gate ("tune out") irrelevant information (Arciniegas et al., 1999). Knight, Staines, Swick, and Chao (1999) hypothesized that sensory gating impairments result from deficits in a prefrontal-thalamic system. Recent research (Grunwald et al., 2003) has suggested that sensory gating depends on the integrity of the hippocampus, temporoparietal areas, and the prefrontal cortex. Presumably due to damage to these areas, individuals with mild head injury have been shown to have sensory gating impairments (Kumar et al., 2005). In their study, Kumar and colleagues showed that sensory gating impairments accounted for 50% of the variance in post-concussive symptoms.

Sensory gating is commonly investigated with electrophysiological methods, particularly ERPs. Alho, Woods, Algazi, Knight, and Naatanen (1994) recorded ERPs to short (50 ms) tones at 1000 Hz (standard) and 1300 Hz (deviant), from individuals with dorsolateral prefrontal lesions and age-matched controls. They reported that the patient group had larger P1 amplitudes to standard stimuli; the authors equated this finding with reduced sensory gating of input from the thalamus to the auditory cortex. Arciniegas and colleagues (1999) also studied the disruption that occurs to the sensory gating system following TBI. They recorded electroencephalography (EEG) to paired auditory stimuli (conditioning and test stimuli). In this first investigation of the P50 in this population, the authors found that each of three participants showed a delayed P50 latency and non-suppression of the test P50. These results are limited by the fact that only three participants were studied, and because these individuals had different injury severities and different mechanisms of injury. However, each participant was chosen because

he/she complained of difficulties with attention. The authors summarized that the clinical correlate of these effects is commonly described as *distractibility*. They further argued that, because this problem results from the inability to filter out irrelevant sensory information, this clinical problem should more appropriately be described as *failure in sensory gating*.

Arciniegas et al. (2000) sought to replicate these findings in a larger sample of individuals with traumatic brain injuries. They again selected participants who complained of problems with attention, with the aim to determine if these difficulties would be reflected in non-suppression of the P50 component. The authors reported that this larger sample (n=20) did show poorer sensory gating, as revealed by non-suppression of the test P50, compared to control participants. Arciniegas et al. (2001) added that sensory gating impairments may result from direct damage to the hippocampus or from damage to cholinergic connections from the basal forebrain to the hippocampus. The hippocampus is important for attention, in that it filters sensory information before it is passed on to the cortex (Arciniegas et al., 1999).

Arciniegas et al. (2001) reported that individuals with TBI who showed P50 non-suppression had disproportionate hippocampal volume loss measured with magnetic resonance imaging, i.e., hippocampal volume was reduced more than could be accounted for by reduction of total brain volume. Finally, Arciniegas and Topkoff (2004) provided a review of the relationship between impaired sensory gating and more general cognitive impairment in TBI. They suggested that a "cholinergic hypothesis" of cognitive impairment in TBI explains both sensory gating and cognitive impairments. Specifically, they cited evidence that cholinergic functioning is altered after TBI, and furthermore

referred to the well-established relationship between cholinergic dysfunction and cognitive impairment. While these deficits in sensory gating have been documented by Arciniegas' group in waking, it is important to determine if similar impairments exist in sleep to explain complaints of insomnia-like symptoms in TBI.

Dysregulation of the Sleep/Wake System in Individuals with TBI

Sleep disturbance and daytime fatigue are common complaints following TBI. Researchers distinguish sleepiness as the propensity to fall asleep and fatigue as physical or mental overload. Most research to date has only described the prevalence of daytime fatigue and insomnia symptoms in this population (see Ouellet, Savard, & Morin, 2004 for review). Daytime fatigue (Ouellet & Morin, 2006; Ziino & Ponsford, 2005) and hypersomnia (Cohen, Oksenberg, Snir, Stern, & Groswasser, 1992) are common in the acute phase of recovery from TBI. Fatigue may occur due to injury of brain regions involved in arousal level, such as the reticular activating system and basal forebrain, which may occur more often in severe injuries. Daytime fatigue may also occur as a consequence of the extended effort put forth when processing speed is impaired (Ziino & Ponsford, 2005) or possibly from disrupted sleep.

Ziino and Ponsford (2005) compared subjective fatigue in 49 individuals with TBI to 49 control participants. TBI participants ranged in injury severity from mild to severe. The authors argued that previous studies using physiological measures of fatigue, such as a thumb pressing task (LaChapelle & Finlayson, 1998) and a reaction time task (Stuss et al., 1989) were not sensitive because they showed no differences between TBI and control participants. Thus, Ziino and colleagues employed all self-report scales to investigate fatigue in a sample of individuals with TBI. Using the Visual Analogue Scale

for Fatigue (Lee, Hicks, & Nino-Murcia, 1991), the Fatigue Severity Scale (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989), and the Causes of Fatigue Questionnaire (Ziino & Ponsford, 2005), the authors found that individuals with TBI reported greater levels of fatigue, and that physical and mental effort resulted in fatigue more often compared to controls. Although the visual analogue scale measured fatigue at a particular point in time, the remaining measures assessed more chronic levels of fatigue, e.g., "Fatigue causes frequent problems for me". Details regarding the time of day at which these measures were completed were not provided. Moreover, results suggested that fatigue had a greater impact with increasing time since injury; although this idea may seem counterintuitive, the authors postulated that as individuals begin to recover, they engage in more activities, causing more fatigue, or become more aware of their fatigue.

In another study using a different self-report measure to examine daytime fatigue in individuals with TBI, Borgaro, Baker, Wethe, Prigatano, and Kwasnica (2005) compared level of fatigue in 45 TBI patients with that in a group of 30 non-injured controls, with the Barrow Neurological Institute Fatigue Scale (Borgaro, Kwasnica, Caples, & Gierok, 2004). Borgaro et al. found that the TBI group reported greater fatigue than control participants. However, fatigue was not related to injury severity, nor to number of days since the injury, cognitive impairment, or gender.

Ouellet and Morin (2006) also used a self-report questionnaire to examine the prevalence of fatigue following TBI. Approximately two-thirds of the 452 participants who completed the questionnaire reported significant fatigue. Specifically, mental fatigue was more problematic than physical fatigue. Fatigue was witnessed in acute stages of recovery as well as several years post-injury, though the authors found that a shorter time

since injury was positively related to greater fatigue. Injury severity did not predict the presence of fatigue. When they investigated the relationship between fatigue and other variables associated with participants' functioning, Ouellet and Morin found that greater fatigue was associated with higher psychological disturbance, greater pain, and greater sleep disturbance. As well, participants reported that fatigue interfered with their day-to-day activities, social/leisure activities, and rehabilitation, and negatively impacted their mood and cognitive abilities (Ouellet & Morin, 2006).

A special issue of the *The Journal of Head Trauma Rehabilitation* in 2008 was dedicated to fatigue following TBI. Bushnik, Englander, and Wright (2008b) investigated the time course of fatigue across the first two years post-injury in 51 participants with a TBI. Fatigue was assessed by self-report. Fatigue diminished in the first year post-injury; notably, other related symptoms such as sleep disturbance, pain, and cognitive ability improved as well. A subset of individuals showed the opposite pattern, however, that fatigue increased through time, and this was associated with poorer outcomes. Bushnik, Englander, and Wright (2008a) also reported that approximately one-quarter to one-third of participants who were surveyed experienced fatigue in the first two years following a moderate to severe TBI. Like Ouellet and Morin (2006), these authors reported that fatigue was related to sleep disturbance. Specifically, participants' scores on the Pittsburgh Sleep Quality Index (PSQI) were highly positively correlated with fatigue scores, even after controlling for fatigue-related items on the PSQI (Bushnik et al., 2008a).

Cantor et al. (2008) compared individuals with TBI ranging in severity from mild to severe to control participants without a TBI. Assessed by interviews and self-report

questionnaires, the authors reported that fatigue was more prevalent in the patient group, and more prevalent in women in both groups. Sleep problems, pain, and depression accounted for 23% of the variance in fatigue in the TBI group, and fatigue was related to quality of life. Given that fatigue was not related to a number of demographic and injury variables, the authors concluded that fatigue was at least partially caused by the TBI directly.

Daytime sleepiness, in contrast to fatigue, is also a common complaint of individuals with TBI and may be more directly linked to sleep impairment. Watson, Dikmen, Machamer, and Temkin (2005 [abstract]) showed that hypersomnia (or excessive sleepiness) following TBI often abates with time following injury, but that it is more likely to persist at higher levels of injury severity. To investigate the level of sleep disruption and daytime sleepiness following TBI, Parcell, Ponsford, Rajaratnam, and Redman (2006) asked participants with TBI and controls to complete a sleep diary for seven days; this diary allowed researchers to assess times that participants went to sleep and awoke, sleep onset latency, frequency and duration of awakenings, and daytime naps. Researchers also administered a questionnaire to assess changes to sleep following the TBI, and used the Epworth Sleepiness Scale (Johns, 1991) to assess daytime sleepiness. Parcell and colleagues reported that 80% of participants reported changes to their sleep following TBI. More specifically, this group reported taking longer to fall asleep, longer to wake up in the morning, poorer sleep efficiency, i.e., time asleep per time in bed, and longer naps, compared to their pre-injury sleep characteristics. Interestingly, the researchers verified that these sleep changes in the TBI group did not result from lifestyle changes in this group, such as being unemployed. Although most studies rely on self-

report measures, there are inherent problems with self-reports. These problems include inaccuracies in memory when required to answer retrospectively, and problems with lost data when participants are required to complete lengthy questionnaires or to keep ongoing logs such as a sleep diary. Parcell et al. suggested that one way to circumvent this limitation is to also use actigraphy as a more objective measure of sleep and activity. Another method would be to verify sleep disturbance with polysomnography.

Although daytime fatigue and sleepiness may abate as an individual recovers from TBI, symptoms of insomnia may begin to develop; insomnia may actually develop due to compensatory strategies employed to combat fatigue, e.g., drinking excessive caffeine, daytime napping. In the first systematic investigation of sleep complaints following minor head injury in 75 individuals, Parsons and Ver Beek (1982) showed, based on questionnaire data, that the number of sleep interruptions per night and the number of nights of interrupted sleep per week were significantly higher following head injury; additionally, the number of nights per month that individuals awoke and could not return to sleep was higher following head injury. As well, more sleep was needed in order for individuals to function efficiently following head injury. Finally, following head injury, individuals complained more about sleep and experienced poorer sleep quality relative to their sleep pre-injury. These effects did not correspond to the anatomical location of the head injury, but were related to both the length of disruption in consciousness that occurred as a result of the head injury and the degree of severity as measured by GCS score.

Cohen et al. (1992) compared self-reported sleep problems of individuals with recent TBIs to those who had sustained a TBI two to three years earlier. They reported

that, overall, 72.7% of the 22 individuals who had recently sustained a TBI complained of sleep problems. Eighty-two percent of these participants complained of difficulty initiating (five participants) or maintaining sleep (seven participants) or both (one participant). Of the 77 individuals who had sustained a TBI in the past, 52% complained of sleep disturbances. In contrast to those with recent TBIs, 73% of these individuals complained of excessive daytime sleepiness and only three individuals reported trouble initiating and maintaining sleep. Neither age nor duration of coma following injury was related to sleep complaints in either group, although more women in each group complained of sleep problems.

Segalowitz and Lawson (1995) examined sleep complaints in high school and university students with mild head injury and those without. In the high school students, they found that, overall, girls had more sleep difficulty than boys, but these difficulties were not related to their reported head injury. Boys, however, were more likely to report difficulty sleeping if they had sustained a head injury. In the university sample, there were no gender differences; difficulty sleeping was reported more often in those with a head injury than those without across men and women. Segalowitz and Lawson asked a subset of their university sample more detail about their sleep problems. Individuals with a mild head injury had more difficulty falling asleep, woke more during the night, and had more trouble falling back to sleep. Individuals with a head injury were not more likely, however, to report waking too early in the morning or to complain of daytime tiredness. Individuals with and without head injury did not differ on total sleep time per night, enjoyment of sleep, or how refreshed they felt upon awakening. Finally,

individuals who had sustained multiple head injuries complained, in general, of more sleep problems.

Beetar, Guilmette, and Sparadeo (1996) investigated sleep complaints in individuals with TBI; they were interested in whether complaints of pain exacerbated insomnia symptoms in this group. The authors reported that individuals with neurologic conditions other than TBI showed the same rate of insomnia as the general population. Insomnia in individuals with TBI, however, occurred almost twice as often. Moreover, across both groups, pain nearly doubled the incidence of insomnia. Finally, although aging is often associated with poor sleep and the presence of insomnia (Bliwise, 2005), insomnia occurred more frequently in the TBI group even though they were younger. In their study of 86 individuals who had sustained a brain injury, Clinchot, Bogner, Mysiw, Fugate, and Corrigan (1998) described that 50% of participants complained of sleep difficulty. Of these participants, 64% complained of early morning awakenings, 45% complained of difficulty falling asleep, and 25% complained of sleeping too much. In addition, 63% of participants complained of fatigue. Sleep difficulties were more likely to occur in older participants and women; additionally, individuals with more severe injuries, based on lower GCS scores, were more likely to indicate that they had sleep problems. Fichtenberg, Zafonte, Putnam, Mann, and Millard (2002) determined that 30% of 50 TBI patients met criteria for insomnia. Participants complained of difficulty initiating sleep twice as often as they complained of short sleep duration. Another 12% of participants had poor sleep, but failed to meet standard criteria for insomnia (DSM-IV; American Psychiatric Association, 2000). This prevalence rate was reported to be higher

than insomnia prevalence in the general population, i.e., approximately 10%, but not higher than that of other medical groups, i.e., 34% to 65% (Fichtenberg et al., 2002).

Ouellet, Beaulieau-Bonneau, and Morin (2006) recently investigated the prevalence of sleep complaints in a large sample of TBI survivors recruited from a rehabilitation facility. The authors reported that approximately half of the 452 participants experienced sleep disturbances, and approximately one-third met diagnostic criteria for insomnia. In fact, sleep onset difficulties reported by participants were so severe that they exceeded diagnostic criteria, i.e., participants, on average, took one hour to fall asleep and had one and a half hours of time awake throughout the night; they experienced these difficulties six nights out of the week, and on average had experienced sleep problems for six years. Ouellet and colleagues also investigated factors that were associated with sleep complaints in this population. They reported that a less severe TBI, the presence of depressive symptoms, pain, and daytime fatigue all predicted the presence of insomnia. However, neither symptoms of anxiety nor time since injury were predictors of insomnia. Ouellet and others mentioned that additional factors, such as duration of coma, size and location of lesions, medications, social support, stress, predisposition to insomnia, and involvement in litigation, should be investigated.

Rao et al. (2008) investigated the prevalence of sleep disturbance in the acute recovery period (up to three months post-injury) following TBI. Rao et al. used the Medical Outcome Scale for Sleep to compare retrospective reports of pre-injury sleep problems with post-injury reports of sleep problems. The authors also examined a number of other variables of interest, namely depression, anxiety, medical complications, and injury severity. They reported that, on average, participants had worse sleep post-

injury. Second, the authors reported a relationship between sleep disturbance post-injury and the presence of anxiety. However, as the authors noted, the direction of this relationship remains unclear.

Since insomnia often involves engaging in compensatory behaviours that ultimately interfere with sleep, e.g., daytime napping, psychologists often utilize cognitive and behavioural strategies to combat insomnia. Ouellet and Morin (2004) studied the effectiveness of cognitive-behavioural therapy for insomnia (CBTi) in one participant who complained of difficulty falling and staying asleep subsequent to sustaining a TBI. Their CBTi treatment protocol produced improvements in sleep quality and quantity for this individual. While this study provided the first information about the usefulness of CBTi in treating individuals with insomnia secondary to TBI, it is necessary to continue to investigate the nature of insomnia in TBI with subjective and objective measures, and to replicate the results of Ouellet and Morin's treatment study with a larger sample.

While a number of studies have emerged in the last decade documenting the prevalence of sleep complaints in TBI patients, few published studies have assessed these complaints objectively. The use of more objective tools allows researchers to more clearly describe the nature of sleep problems following TBI. Makley et al. (2008) documented a high degree of sleep disturbance in 31 individuals with a closed head injury who were patients in a rehabilitation unit. They noted that sleep disturbance was associated with longer stays in rehabilitation settings. A subsequent study used actigraphy to more objectively examine sleep problems in TBI patients (Makley et al., 2009). The authors were interested in determining if length of PTA (an indicator of injury severity

often used to predict post-injury outcomes) was related to sleep efficiency as measured by actigraphy in the immediate period following TBI. In the first week post-injury, 78% of participants had sleep efficiency scores of 63% or lower (note that sleep efficiency for good sleepers is typically above 85%). Participants with PTA that had resolved before admittance to hospital had better sleep efficiency scores than those with ongoing PTA (Makley et al., 2009). This suggests that sleep parameters can be used as an index of recovery.

A limited number of studies have used polysomnography to describe the sleep architecture of individuals with TBI. Several older reports employed individuals with severe brain injuries. Grossman (1949) studied individuals who had unilateral brain damage. Auditory stimuli were presented to both individuals with brain injury and a control group who were asleep through sedation. Importantly, while K-complexes were equivalent in both hemispheres for the control group, the K-complex response to stimuli was reduced over the injured region in the brain injury group (Grossman, 1949). Colrain (2005) noted that Grossman's evidence was so clear that the K-complex method was even used to diagnose a right frontal brain lesion in a patient, which was later confirmed at autopsy.

Lenard and Pennigstorff (1970) recorded the sleep of children who had sustained head injuries at two timepoints: (1) within five days of the injury; and, (2) one to three weeks after the injury. The authors reported that these children had more light sleep and less deep sleep, with no differences in rapid eye movement (REM) sleep during the first recording night compared to the second night. There were, however, more rapid eye movements during REM sleep on this first night. There was also more non-REM

(NREM) sleep with sleep spindles than without, and spindle duration was longer immediately following the injury. It is plausible that the increase in rapid eye movements and sleep spindles reflect a type of recuperation or compensatory mechanism. Given recent research linking both REM and sleep spindles to learning and memory (e.g., Fogel, Smith, & Cote, 2007; Smith, 1995), increases in these phasic events may reflect extra time and/or neural processing needed to consolidate memories. These events may also reflect a process of neural recovery after the head injury.

Harada, Minami, Hattori, Nakamura, and Kabashima (1976) used polysomnography to examine the sleep of 105 adults with severe brain injuries resulting from various causes. Although there was large variation in their sleep, several trends were common among participants. First, participants with severe brain damage showed shorter total sleep times and disrupted sleep. They also had less deep sleep, and fewer vertex sharp waves and sleep spindles; in many participants, these phasic events had completely disappeared. K-complexes were also reduced. The presence or absence of REM sleep seemed to depend on the etiology of the brain damage. Finally, Harada and colleagues reported that abnormal EEG, e.g., EEG spiking, and indeterminate sleep stage, i.e., mixture of sleep and wakefulness, occurred in a number of these severely-injured participants.

In a study using recordings of night sleep EEG on three different occasions across the first year of recovery from severe head injury, George and Landau-Ferey (1986) showed that slow wave sleep (SWS) remained stable throughout the year. Nighttime awakenings were higher for participants with a head injury than control participants at one month post-injury, lower at six months and higher again at one year post-injury.

Likewise, REM sleep was lower at one month, higher at six months (although still lower than that seen in controls), and lower again at one year; lower REM amounts at one year post-injury resulted from shorter REM periods, rather than from fewer REM periods.

In an investigation of individuals with severe brain injuries in the post-recovery period (mean time since injury=6 years), Manseau (1996 [abstract]) compared 16 individuals with TBI to matched controls. He reported that patients who complained of daytime sleepiness showed symptoms of both sleep-onset insomnia and sleep-maintenance insomnia during an all-night recording, and also showed evidence of trouble falling asleep during the daytime multiple sleep latency test (MSLT; Carskadon & Dement, 1977).

In a recent laboratory investigation, Kaufman et al. (2001) recorded the sleep of 19 adolescents who had sustained a mild head injury and complained of sleep disturbances. Questionnaire data comparing individuals with mild head injury and healthy adolescent controls matched for age showed that the patient group had longer sleep latencies, more early morning awakenings, more restless sleep, and greater daytime sleepiness. Sleep talking and bruxism were also more common among the patient group, although somnambulism was more common in the control group. Interestingly, questionnaire data showed that the patient group experienced fears of going to sleep, fearful awakenings from sleep, and frightening dreams. The authors reported that the participants' self-reported sleep problems were corroborated by polysomnographic recordings, which showed lowered sleep efficiency (time asleep per time in bed), more time awake, and more frequent long awakenings during the night. Finally, actigraphic recordings also showed that adolescents with mild head injury had lower sleep efficiency,

more minutes awake, and more long awakenings. As well, participants in the patient group fell asleep earlier and woke later than control participants. It should be noted that these findings are based on recordings from the participants' first night in the laboratory (Kaufman et al., 2001), and therefore the "first night effect" cannot be ignored. The first night effect refers to the idea that sleep will differ due to changes in the environment, which occur when sleeping away from home in a sleep laboratory, motel, or another unfamiliar location (Agnew, Webb, & Williams, 1966). Several pieces of evidence, however, argue against the idea that the first night effect confounded the results. First, control participants were also recorded on their first night in the laboratory, but group differences in the predicted direction still emerged. Second, questionnaire and actigraphic data, which are not subject to the first night effect, were consistent with polysomnographic findings. Third, poor sleepers often experience a reverse first night effect, characterized by better-than-normal sleep away from home, but this pattern was not seen for the head injury group.

Schreiber et al. (2008) used both polysomnography and the MSLT to compare sleep disturbances in 26 individuals with "minor" TBI to healthy matched controls. Participants' sleep was recorded over two nights, but only data from the second night were analyzed, to eliminate the first night effect. Participants with a TBI had significantly more Stage 2 sleep and less REM sleep, but no differences were found for other stages of sleep or sleep stage latencies (Schreiber et al., 2008). Individuals with a TBI also had less total sleep time (Schreiber et al., 2008). During the MSLT, participants with a TBI fell asleep more frequently and more quickly (Schreiber et al., 2008). In general, there is some evidence that individuals with a minor TBI have a dysregulation in their sleep/wake

system, such that they show evidence of lighter sleep through the night, and more sleepiness in the daytime.

Few studies have used quantitative EEG to investigate sleep and arousal in individuals with TBI. One earlier report (Tebano et al., 1988) of waking EEG measured with eyes closed in individuals with head injury showed higher theta and low-alpha power and lower high-alpha and beta power, compared to matched controls. Overall, these differences show EEG slowing in individuals with head injury, suggesting increased sleepiness in this group. A second study of waking EEG in individuals with mild head injury found increased coherence among electrode sites at frontal regions and more similarity in power between anterior and posterior sites, but less alpha power at posterior sites, compared to controls (Thatcher, Walker, Gerson, & Greisler, 1989). These EEG differences may reflect compensatory mechanisms of the brain. To manage the demands of waking tasks, there may need to be recruitment of additional cortical areas, reflected in the increased coherence of various areas in individuals with a TBI. Differences in alpha activity may reflect the notion that individuals with a TBI were not as relaxed as controls.

Parsons, Crosby, Perlis, Britt, and Jones (1997) provided one of the only quantitative EEG studies of the sleep of individuals with minor head injury. Power spectral analyses were computed on four bipolar recordings of the sleep EEG of individuals with head injury on three occasions, one night 72 hours after the injury, the second night 6 weeks after the injury, and the third night 12 weeks after the injury. In their investigation of the sleep EEG of eight adolescents with minor head injury, Parsons et al. showed that delta, theta, and low-alpha power were all increased on the first

recording night compared to the second and third nights. On the second night, theta power at frontotemporal sites during the first REM period had decreased. On the third night, theta and low-alpha power at frontotemporal sites in the first REM period decreased, delta, theta, and low-alpha power at frontotemporal sites in the second REM period decreased, and delta and theta power at temporal sites during the second REM period decreased. The decreases in delta and theta on the second and third nights likely represent impairments in sleep homeostatic processes.

Given the close relationship between Process S and delta power, it is plausible that the reductions in delta and theta power reflected disruptions in the patients' abilities to regulate sleep and wakefulness states. These changes may also reflect impairment in EEG slowing, in contrast to Tebano et al.'s (1988) waking data; in sleep, a lack of EEG slowing would cause an inability to achieve deep sleep. Although these results are interesting, this study could have been enhanced by utilizing a larger sample size and using a healthy control group.

Williams, Lazic, and Ogilvie (2008) also provided a report of polysomnographic and quantitative EEG (qEEG) differences in individuals with a mild TBI (MTBI) and those without. MTBI participants were required to be between six months and six years post-injury, to have neurotrauma indicators of injury, e.g., PCS symptoms, and to have altered sleep/wake patterns post-injury that were consistent with the onset of insomnia soon after the injury. Participants had their sleep recorded in the lab across three nights. Polysomnographic data from the third night and qEEG data from the sleep onset period of the same night were analyzed. The MTBI group had less efficient sleep, shorter REM latencies, longer sleep onset latencies, and more variable sleep (note that variability in

qEEG was quantified by analyzing the standard deviation of power in various frequency bands across the sleep onset period divided into quartiles). As well, qEEG data showed that MTBI participants had higher variability in delta, theta, and sigma power during sleep onset. This variability in sleep parameters is consistent with studies of the night-to-night variability in patients with insomnia (e.g., Vallieres, Ivers, Bastien, Beaulieu-Bonneau, & Morin, 2005).

Although the authors sought to characterize MTBI participants' sleep into one of the well-established insomnia subtypes (psychophysiological, psychiatric, idiopathic), they were unable to do so (Williams et al., 2008). Specifically, the authors noted that idiopathic insomnia is characterized by reductions in SWS and increases in REM, but they did not find this pattern with the TBI group, compared to controls. Second, Williams et al. did not observe the same pattern of qEEG that was found in a study of psychophysiological and psychiatric insomniacs in the same laboratory (Lamarche & Ogilvie, 1997). The TBI group scored higher than controls on questionnaire data used to evaluate *both* psychophysiological and psychiatric insomnia, preventing Williams et al. from binning individuals with a TBI into an insomnia subtype.

Very recently, athletes with a history of concussion were studied with questionnaires, polysomnography (PSG), and qEEG (Gosselin et al., 2009). As expected, concussed participants reported more symptoms of sleep disruption and worse quality sleep compared to non-concussed participants. However, Gosselin and colleagues did not find differences in PSG or qEEG during the night. A methodological problem with Gosselin et al.'s study may have arisen due to the fact that they binned all NREM sleep stages together across the night for their qEEG analyses. A better approach would be to

investigate qEEG differences in each sleep stage separately, e.g., evidence of hyperarousal might only be witnessed in lighter or earlier Stage 2 sleep; evidence of disruption to sleep homeostatic processes might only be witnessed in deeper Stage 4 sleep. Despite the lack of differences in sleep EEG, Gosselin and colleagues did detect differences in the waking power spectra. Specifically, the presence of a concussion was related to more delta power and less alpha power during wakefulness on the second night in the laboratory. An interesting question is whether these waking differences would also exist at other times during the day, rather than just at the sleep onset period.

In a recent review of sleep disturbance in TBI, Orff, Ayalon, and Drummond (2009) acknowledged previous research for consistently documenting the presence of insomnia complaints in those with TBI, and for using adequately large sample sizes. Orff et al. also recognized that the objective study of sleep disruption after TBI has been relatively scarce. They listed small sample size, varying participant ages between studies, and varying injury severity of participants within and between studies as contributing factors to equivocal findings and null results (Orff et al., 2009). Finally, Orff and colleagues recognized the benefits of recent research investigating neurophysiological disruptions in the regulation of sleep and wakefulness. Baumann and colleagues have recently launched a series of studies investigating changes in hypocretin following TBI. Hypocretin is a neuropeptide produced in the hypothalamus that promotes wakefulness. Baumann et al. (2005) found lower hypocretin-I in 95-97% of individuals with an acute moderate to severe TBI compared to controls. In a follow-up study, Baumann, Werth, Stocker, Ludwig, and Bassetti (2007) replicated their results with acute TBI, but found that only 4 out of 21 participants had lower hypocretin-I levels six months post-injury.

The latter data may have been influenced by the fact that the authors included individuals with varied injury severities (Baumann et al., 2007). Baumann et al. (2007) also reported that reduced hypocretin-I levels were associated with excessive daytime sleepiness. Orff et al. remarked that these data may reflect damage to the hypothalamus, which houses hypocretin neurons, and remarked that the data certainly explain the incidence of daytime fatigue following TBI.

In a more general review of alterations in the hypocretin system, Fronczek, Baumann, Lammers, Bassetti, and Overeem (2009) postulated that the change in hypocretin-I levels immediately after TBI may result from down regulation of hypothalamic hypocretin neurons and/or diffuse axonal injury of hypothalamic tracts. They further stated that neuronal death of hypocretin neurons was supported by exploratory work that showed reductions in hypocretin neurons in TBI patients at autopsy, compared to non-injured controls (Fronczek et al., 2009). Importantly, Fronczek et al. appropriately connected the loss of hypocretin neurons to the presence of excessive sleepiness and post-traumatic narcolepsy. While their findings may help to explain post-traumatic fatigue, the neurophysiological underpinnings of insomnia-like symptoms post-injury are unknown.

Chapter 4: Rationale and Hypotheses

Traumatic brain injury (TBI) is associated with daytime fatigue and sleep disturbance. Studying sleep in individuals with a TBI is important because sleep disturbance likely exacerbates other symptoms of TBI, such as pain, cognitive impairments, and emotional disturbances (Ouellet & Morin, 2004; Ouellet et al., 2004; Thaxton & Myers, 2002), and may impede recovery (Fichtenberg, Millis, Mann, Zafonte, & Millard, 2000). Patient reports, clinical observation, and survey research have identified that sleep is a major problem for those with a TBI (see Ouellet et al., 2004; Orff et al., 2009 for reviews). However, there is little research using polysomnography (PSG), quantitative electroencephalography (qEEG) and/or event-related potentials (ERPs) to understand sleep in TBI from a neurophysiological perspective. In general, these quantitative measures were employed in this dissertation in order to understand sleep in TBI. More specifically, it was hypothesized that sleep complaints in TBI could be explained by a breakdown in sleep/wake regulation, alterations in information processing and sensory gating, and the presence of hyperarousal.

Hypothesis 1. The few studies that have investigated sleep in a TBI group in the laboratory (George & Landau-Ferey, 1986; Harada et al., 1976; Kaufman et al., 2001; Lenard & Pennigstorff, 1970; Manseau, 1996; Schreiber et al., 2008; Williams et al., 2008) have shown with sleep architecture that individuals with TBI have poorer sleep, including reduced sleep efficiency and lighter sleep. Based on such reports, a goal for this study was to replicate these findings and confirm that participants with TBI had poorer sleep than controls as measured with sleep architecture. For example, as seen in previous research, compared to controls, those with a TBI were expected to have reduced sleep

efficiency, delayed sleep onset, more wake time after sleep onset, less deep sleep and more light sleep, reflecting less efficient and less restorative sleep.

Hypothesis 2. Several earlier studies investigated sleep phasic events in individuals with TBI. Neurobiological studies (Amzica & Steriade, 2000; Steriade, 2000) have suggested that both the sleep spindle and K-complex reflect inhibitory processes occurring in thalamocortical networks. Grossman (1949) showed a reduction in the elicitation of K-complexes over the hemisphere of brain damage, in comparison to bilateral elicitation in a control group. Lenard and Pennigstorff (1970) showed that sleep spindles were increased in number and duration in the acute phase of recovery, while Harada et al. (1976) showed that both sleep spindles and K-complexes were reduced in number. Given that it was expected that individuals with a TBI would show a breakdown in inhibitory processes, it was hypothesized that individuals with a TBI would have fewer K-complexes and sleep spindles than controls.

Hypothesis 3. Relatively few studies have used qEEG techniques to investigate arousal levels in wakefulness and sleep in those with a TBI. Using qEEG in wakefulness, both Tebano et al. (1988) and Gosselin et al. (2009) reported excessive EEG slowing in individuals with a head injury, a notion consistent with reports of excess fatigue (e.g., Borgaro et al., 2005; Bushnik et al., 2008a,b; Cantor et al., 2008; Cohen et al., 1992; Ouellet & Morin, 2006; Ziino & Ponsford, 2005). Thatcher et al.'s (1989) qEEG research suggested that individuals with a mild head injury needed to recruit additional cortical areas during wakefulness. This inefficient information processing is also consistent with the notion that individuals with a TBI suffer from daytime fatigue.

Whereas the studies described above examined qEEG in those with a TBI in wakefulness, importantly, Parsons et al. (1997) examined qEEG during sleep in adolescents with head injury. Their results suggested impaired sleep homeostatic mechanisms, providing support for the poor sleep that accompanies TBI. In this dissertation, qEEG was used to investigate both impairments in sleep homeostatic mechanisms and the presence of hyperarousal. Due to the lack of research examining hyperarousal in TBI, models of insomnia were used, given the prevalence of insomnia complaints in TBI.

Previous research investigating the concept of hyperarousal showed that individuals with insomnia had elevated metabolic rates during the day (e.g., Bonnet & Arand, 1997). The more recent neurocognitive model of insomnia (e.g., Perlis, Smith, & Pigeon, 2005) has provided evidence in support of a central nervous system hyperarousal. Given this model of insomnia and the prevalence of insomnia complaints after TBI, it was hypothesized that individuals with a TBI would show evidence of neurocognitive hyperarousal. Specifically, individuals with a TBI were expected to have greater beta and gamma power during sleep, reflecting sleep disruption. Second, given Parsons et al.'s data suggesting impairments in sleep/wake regulation, it was hypothesized that participants with a TBI would show evidence of sleep homeostatic impairments. Specifically, based on Borbely et al.'s (1981) research outlining that delta power in sleep reflects the homeostatic process, individuals with a TBI were expected to have lower delta power during sleep than age-matched controls, reflecting disruptions to sleep homeostatic mechanisms. With respect to qEEG in wakefulness, it was expected that the EEG slowing previously reported in a sample of individuals with head injury would

characterize a subset of our sample, i.e., individuals with a TBI who complained of daytime fatigue. Given the presence of hyperarousal in insomnia, however, it was also expected that increased high frequency activity might be evident in a different subset of the sample, i.e., individuals with a TBI who complained of insomnia.

Hypothesis 4. No researchers to date have used ERPs during sleep to investigate information processing in TBI. In this dissertation, both a paired-click and a pitch oddball paradigm were used to investigate sensory gating and information processing, respectively, in both wakefulness and sleep. The paired-click paradigm is used to elicit the P50 component to two identical stimuli. Suppression of the response to the second stimulus represents intact gating (Adler et al., 1982; Waldo & Freedman, 1986). Kisley et al. (2001, 2003) have shown that intact gating in waking remains intact in REM sleep, while impaired gating in waking is also impaired in REM sleep. Our own research (Milner, Cuthbert, Kertesz, & Cote, 2009; see Appendix A) has shown that sensory gating is impaired during the pre-sleep waking period in poor sleepers. Based on these studies and previous research documenting that individuals with a TBI have impairments in sensory gating during waking (Arciniegas et al., 1999, 2000, 2001; Arciniegas & Topkoff, 2004), it was hypothesized that participants with a TBI would show non-suppression of the P50 in both wakefulness and sleep, reflecting impairments in sensory gating.

The pitch oddball paradigm elicits the N1 and P2 components to standard stimuli, and the N1-P2-P300 complex to target stimuli in waking (Picton, 1992). ERP studies of waking performance have shown that individuals with a TBI are cognitively slower (Lew et al., 2004), are less able to appropriately allocate attention (Rugg et al., 1993;

Segalowitz et al., 2001; Solbakk et al., 2002), and are less able to inhibit irrelevant information (Solbakk et al., 1999). Thus, it was expected that individuals with a TBI would have impairments in information processing in wakefulness, thereby confirming previous results. While no research exists with respect to these components in TBI in sleep, the change in the ERP from waking to sleep is well-documented in good sleepers. The N1 and P2 are overlapped in space and time by a processing negativity wave; during sleep onset, the removal of this attention-dependent wave decreases N1 and increases P2 and represents the engagement of inhibitory processes that are thought to promote sleep (Campbell & Colrain, 2002; Cote et al., 2002; de Lugt et al., 1996), whereas the P300 only exists at sleep onset and in REM sleep in response to salient stimuli (Cote & Campbell, 1999a,b). Finally, many waking ERP components disappear, and are replaced by components specific to sleep (e.g., Harsh et al., 1994).

Given the insomnia-like complaints of individuals with a TBI, it was important also to have an understanding of waking and sleep ERPs in insomnia. Devoto, Violani, Lucidi, and Lombardo (2003) measured waking ERPs to pitch oddball stimuli following both a bad and a good night of sleep in a group of insomniacs. Participants with insomnia had larger P300 amplitudes at frontal sites than good sleepers following poor nights. Devoto et al. (2005) replicated these findings, but also reported that larger P300 amplitudes were visible in the evening prior to a bad night of sleep. Yang and Lo (2007) reported that poor sleepers had larger N1 amplitudes and smaller P2 amplitudes, suggesting hyperarousal and impaired inhibition. Poor sleepers also had a smaller N350 amplitude, which is a sleep-specific waveform associated with inhibition during sleep. Finally, Bastien, St-Jean, Morin, Turcotte, and Carrier (2008), consistent with Yang and

Lo, reported that poor sleepers had a larger N1 amplitude during wakefulness both before and after a night of sleep. During sleep onset, poor sleepers had a smaller N1 and larger P2 amplitude, which contradicts both the waking data and Yang and Lo's findings. Poor sleepers also had a smaller N350, which is consistent with Yang and Lo and with the idea of hyperarousal. A subsequent study by Turcotte and Bastien (2009) showed that larger N1 amplitudes in the evening were related to more wake time after sleep onset and to reduced sleep efficiency. However, larger P2 amplitudes were correlated with reduced sleep efficiency.

These data provide some support for the neurocognitive model of primary insomnia. Based on studies of impairments in TBI in wakefulness, and studies of ERPs in insomnia in sleep, it was hypothesized that pitch oddball ERPs would show that individuals with a TBI have impairments in early encoding and later information processing. Specifically, N1 was expected to be larger and P2 to be smaller and it was expected that both components would be earlier, suggesting over-processing of stimuli and impaired inhibition in sleep. It was also predicted that the P300 would be evident in REM sleep in the TBI group but not the control group, providing evidence that information processing gates were weaker in individuals with a TBI.

Hypothesis 5. Moreover, participants spent two consecutive uninterrupted nights in the laboratory. Whereas previous researchers have not investigated night-to-night variability in TBI, several studies have shown that sleep is more variable in a host of applied populations. In particular, individuals with insomnia show high variability in sleep parameters from night-to-night (e.g., Edinger, Marsh, McCall, Erwin, & Linniger, 1991; Vallieres et al., 2005). For example, Edinger et al. showed with objective and

subjective parameters that all three study nights were variable, even though participants' sleep was recorded at home. Based on the notion of night-to-night instability in sleep, it was hypothesized that participants with a TBI would have more variability from night-to-night than controls, as a reflection of impairments in sleep/wake regulation. This sleep/wake dysregulation predicted greater absolute differences between parallel measures taken on the two recording nights, e.g., greater differences in sleep architecture and phasic events.

Hypothesis 6. TBI frequently results in permanent impairments in cognitive, behavioural, and emotional functioning (Bamdad et al., 2003; Busch et al., 2005). In this dissertation, neuropsychological and laboratory-based behavioural and subjective measures were used to compare the daytime functioning of individuals with TBI to control participants. Based on previous reports of waking function impairments (e.g., Asloun et al., 2008; Mathias, Beall et al., 2004; Rugg et al., 1993; Segalowitz et al., 2001), it was expected that individuals with a TBI would be more impaired than controls. Specifically, it was hypothesized that individuals with a TBI would show evidence of poorer neuropsychological performance, poorer accuracy and slower reaction times on laboratory-based measures, and worse mood and elevated sleepiness as measured by subjective report.

Hypothesis 7. Finally, although no studies to date have systematically investigated the relationship between sleep impairment and waking function in TBI, it is generally accepted that sleep disruption may contribute to waking cognitive and social-emotional deficits apparent in TBI. For example, Ouellet and Morin (2006) showed that fatigue was associated with psychological disturbance, pain, activities of daily living,

social activities, mood, and cognitive abilities, in individuals with TBI. Given that the authors also noted that fatigue was related to sleep disturbance, it is plausible that there is also a connection between sleep impairment and these negative waking function outcomes. Based on the idea that sleep and waking function are related, it was hypothesized that sleep impairment in individuals with a TBI as measured with PSG, sleep phasic events, qEEG, and ERPs would be related to waking dysfunction, while no such association would be seen with controls. Specifically, it was expected that indices of disrupted sleep would be correlated with poor waking function in individuals with a TBI but not controls, and that relationships between sleep and waking function typical of controls would be absent in those with a TBI.

Chapter 5: Method

Pilot Study

A pilot study was conducted to investigate sensory gating in good and poor sleepers. The paired-click paradigm was utilized to elicit the P50 event-related potential component during pre- and post-sleep wakefulness and in each stage of sleep. Results showed that poor sleepers had impaired sensory gating in the pre-sleep waking period. The published study (Milner et al., 2009) can be found in Appendix A.

Participants

Participants were recruited by posters placed around Brock University; through the departmental research pool website (http://brocku.sona-systems.com); through announcements in local newspapers; and, through connections with community organizations and Psychologists' offices. See Appendix B for an overview of the screening criteria. Potential participants contacted the Sleep Research Laboratory via telephone, at which time they completed a brief telephone interview (see Appendix C). The interview screened participants for eligibility criteria, including questions related to their health and sleep. Sixty-three individuals who met screening criteria and who were interested in participating were invited to the laboratory to participate in an orientation session, where they were given a tour of the laboratory, provided informed consent, completed a hearing test, and were asked to complete screening questionnaires. Ten participants were excluded at this point: two participants had complicating factors related to their traumatic brain injury (TBI) that prevented them from being able to participate, i.e., neuromuscular impairments prevented them from being able to complete performance testing; two participants disclosed on questionnaires that they were taking

medications; one participant disclosed on the sleep/wake questionnaire that she had been diagnosed with sleep apnea; and, five participants were no longer interested or could not comply with schedule requirements. All participants' hearing was within normal range, i.e., below 15 dB ISO at 500, 1000, 1500, and 2000 in both ears.

Remaining participants spent one night in the Sleep Research Laboratory to verify that they did not have any major sleep disorders, such as sleep-disordered breathing or periodic limb movements. Five TBI and three control participants were excluded because their sleep records indicated that they had periodic limb movements during sleep. Two other control participants withdrew after the screening night because they could not meet the demands of the remaining study schedule.

At the completion of the testing session, participants were given a sleep and activity diary to be completed for at least one week. The diary data were verified to ensure that participants maintained regular sleep/wake schedules, used minimal caffeine, and refrained from napping. No participants were excluded for non-compliance.

Forty-three participants completed the full study protocol. Three of these participants were not used in the final data set. One participant in the control group was found to have periodic limb movements during his screening night; because the severity of the movements was just at the threshold for exclusion from the study, he was asked to participate in the remainder of the protocol. Further data gathered from leg movement recordings on the three protocol nights confirmed the presence of periodic limb movements, thus he was excluded from data analysis. A second control participant became ill on the third night, and was thus excluded from all data analyses. Finally, a third participant was excluded because her brain injury was qualitatively different than

the other participants in the TBI group, i.e., she had sustained an acquired brain injury due to an anoxic event, while the other participants had all sustained traumatic brain injuries from motor vehicle collisions, sports accidents, falls, or assault.

Data were collected from 40 participants; of these, 20 individuals had sustained a traumatic brain injury and 20 good sleepers were age-matched controls. There were 11 women and 9 men in the TBI group, and 10 women and 10 men in the control group. Most participants were right-handed. However, there was one left-handed person in the control group, and two left-handed persons in the TBI group. See Table 1 for eligibility criteria data for each participant and Appendix D for information about the final sample.

A range of TBI severity was targeted for this study. TBI participants were characterized as having a mild, moderate, or severe TBI based on length of loss of consciousness and/or post-traumatic amnesia, i.e., the longer of these two criteria formed the basis for severity grouping (Williamson et al., 1996). In total, there were 6 individuals with a mild TBI, 8 with a moderate TBI, and 6 with a severe TBI. Participants were also assigned a numerical score from 0 to 20 representing injury severity, which was comprised from their responses during a semi-formal interview with the researcher; participants provided subjective information about length of loss of consciousness, retrograde and post-traumatic amnesia, and neurodiagnostic indicators of injury severity, e.g., vomiting, headache, dizziness, seizuring. Scores that were assigned to participants ranged from 4 to 15 (M=10.90, SD=3.64). These ratings did not directly coincide with the injury rating on which individuals were placed in the three injury severity groups.

Participants in this study were not recruited based on sleep complaint. They

Table 1

Eligibility Criteria and Demographic Information for Each Participant

	Controls		*TBIs*								
ID	Sex	Age	Sex	Age	Sleep Complaint	Injury Severity	Severity Score[1]	Smoker	Medications	Pain	Depression
1	F	18	F	18	Insomnia	Moderate	9	N	N	N	N
2	F	18	F	18	Fatigue	Moderate	15	N	N	N	N
3	F	19	F	18	None	Moderate	12	N	N	N	N
4	F	19	F	18	Fatigue	Moderate	11	N	N	N	N
5	F	20	M	20	None	Mild	10	N	N	N	N
6	M	20	F	20	Fatigue	Mild	14	N	N	N	Y
7	F	21	F	20	Fatigue	Severe	12	Y	N	Y	Y
8	F	21	F	22	None	Severe	10	N	N	N	N
9	F	22	M	22	Insomnia	Mild	5	N	Hypnotic	N	N
10	F	24	F	23	Insomnia	Mild	4	N	N	N	N
11	M	24	F	23	Insomnia	Severe	15	Y	N	N	N
12	F	24	M	25	Insomnia	Moderate	10	N	N	N	N
13	M	25	M	27	Insomnia	Severe	13	N	N	N	N
14	M	27	M	29	Insomnia	Moderate	12	N	N	Y	N
15	M	33	F	34	Insomnia	Moderate	6	N	Hypnotic	N	N
16	M	40	M	43	None	Mild	4	N	N	Y	N
17	M	42	F	43	Fatigue	Moderate	14	Y	N	Y	N
18	M	54	M	51	Fatigue	Mild	14	N	N	Y	Y
19	M	56	M	57	Insomnia	Severe	15	N	N	N	N
20	M	61	M	64	Insomnia	Severe	13	N	N	Y	N

Note. [1]Severity score out of 20.

varied in presence and nature of sleep complaint. Ten individuals reported trouble getting to and/or maintaining sleep ("insomnia" sub-group); six individuals reported daytime fatigue ("daytime fatigue" sub-group); and, four individuals reported no difficulties with sleep or fatigue ("no complaints" sub-group). No relationship was found between injury severity and sleep complaint category, $X^2(4)=1.99$, $p=.70$.

Three TBI participants were casual smokers who reported no difficulty refraining from smoking for the length of each overnight session. Two TBI participants took hypnotic medications for the sleep problems on an as needed basis. A two-week washout period free from these medications was required of these participants before their enrollment in the study. Given the nature of the cause of the brain injury for many TBI participants, e.g., motor vehicle collision, fall, sports injury, assault, a number of participants ($n=6$) self-reported ongoing pain issues during the telephone interview. Control participants all reported being free of pain. While TBI participants were required to be free of premorbid psychiatric disorders, during the telephone interview three TBI participants self-reported symptoms of depression that had occurred since the TBI.

Level of stress across the previous month, measured with the Perceived Stress Questionnaire (PSQ; Levenstein et al., 1993), did not differ between groups. Morningness-eveningness tendency (Horne & Ostberg, 1976) was also similar for the two groups. However, level of fatigue measured with a checklist-typĕ questionnaire (Yositake, 1978) was greater for TBIs[1] who reported daytime fatigue ($M=17.83$, $SD=3.43$) than their matched controls ($M=5.17$, $SD=2.93$), $t(5)=-7.69$, $p=.001$.

[1] [1] While we recognize that the proper terminology is "individuals who have sustained a traumatic brain injury", we have taken the liberty of using the acronym "TBIs" to describe this group with respect to the results in order to be concise.

With respect to mood variables, TBI participants who reported daytime fatigue (M=16.17, SD=9.04) had higher scores on the Beck Depression Inventory (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) than their matched controls (M=5.17, SD=3.06), $t(5)$=-3.24, p=.02. TBIs with daytime fatigue (M=11.92, SD=6.77) also had higher scores on the Beck Anxiety Inventory (Beck, Epstein, Brown, & Steer, 1988) than their matched controls (M=2.33, SD=1.63), $t(5)$=-3.44, p=.02. As well, there was a trend for mild TBIs (M=13.42, SD=8.22) to be more anxious than their matched controls (M=3.67, SD=3.88), $t(5)$=-2.26, p=.07; moderate TBIs (M=4.88, SD=3.56) were significantly more anxious than their matched controls (M=2.25, SD=1.67), $t(7)$=-2.63, p=.03.

Materials

Questionnaires. Questionnaires completed during the orientation session included the IPIP-NEO personality inventory (available from http://ipip.ori.org), Perceived Stress Questionnaire (PSQ; Levenstein et al., 1993), fatigue questionnaire (Yositake, 1978), Beck Depression Inventory (Beck et al., 1961), Beck Anxiety Inventory (Beck et al., 1988), West Haven Yale Multidimensional Pain Inventory (WHYMPI; Kerns, Turk, & Ruddy, 1985), and morningness/eveningness questionnaire (Horne & Ostberg, 1976). These questionnaires were used to determine participant eligibility with respect to stress, fatigue, mood, and pain, and to collect data to compare groups on these measures. No participants were excluded on the basis of these questionnaires. During the orientation session, participants also completed questionnaires that were used to collect demographic information and sleep/wake habits and history (Appendix E). Three participants were excluded based on the sleep/wake questionnaire; two participants

reported taking psychiatric medications, and one participant disclosed she had been diagnosed with sleep apnea.

Sleep diary. Approximately one week prior to the first protocol night, participants were given a sleep and activity diary (Appendix F) to be completed until the end of the study. Diary data were verified on the first protocol night to ensure that participants maintained regular sleep/wake schedules. The mean number of days the diary was completed was 6.75 days for the TBI group, and 8.50 for the control group. Participants provided information about their times to go to sleep and awake, the amount of caffeine consumed, and significant activities such as meals and exercise. Sleep efficiency (time asleep per time in bed) calculated from subjective reports did not differ between the TBI (M=83.30%, SD=11.61) and control groups (M=85.70%, SD=6.87), $t(10)=0.52$, $p=.61$. Data were not available from four TBIs and six controls because their responses failed to discriminate between estimates of time in bed from time asleep. Caffeine usage (number of cups per day) also did not differ between TBI (M=1.12, SD=0.58) and control groups (M=0.85, SD=0.74), $t(19)=-1.32$, $p=.20$.

Pre- and post-sleep questionnaires. Participants completed pre- and post-sleep questionnaires (Appendices G and H) before and after each night in the laboratory. Both questionnaires asked participants to rate the quality of their sleep on the previous night, and to estimate their sleep onset latency, total sleep time, and number of awakenings the previous night. The questionnaires also asked participants to rate their mood, sleepiness, fatigue, physical symptoms, and pain at present.

Analyses were conducted on both a visual analogue "best-worst" rating of sleep quality, as well as a composite score derived from participants' responses on a series of

visual analogue scales that allowed them to rate the quality of sleep onset, sleep through the night, and morning awakening. As well, analyses were conducted on visual analogue mood scales for calm-irritable, happy-sad, energetic-sluggish, and relaxed-tense dimensions. Scores on seven-point sleepiness and fatigue scales were also analyzed. Finally, participants' estimates of sleep onset latency, total sleep time, and awakenings were analyzed. Ratings of physical symptoms and pain were inspected to ensure that no data should be excluded based on extreme levels of physical discomfort. No data were excluded for this reason.

Performance assessment battery. Tasks that comprised the performance assessment battery were presented to participants on personal computers in a private bedroom within the sleep laboratory. E-Prime stimulus delivery software (Psychology Software Tools, Inc.) was used for these tasks. Participants were introduced to several of these tasks (n-back working memory task, Novel P3 task, visual reaction time task) during the orientation session and were able to practice the tasks during the screening night and neuropsychological testing sessions, as well as on the first protocol night. Such an extensive practice was required for the more difficult tasks because cognitive impairments in the TBI group may have prevented them from learning at the same rate as controls. These particular tasks were expected to require several trials to overcome the learning curve inherent in the tasks. Prior to data collection, participants' performance was verified to be adequate, and participants verified their understanding of task instructions. Performance assessment batteries were completed pre- and post-sleep on each of the recording nights. Each performance assessment battery lasted approximately 45 minutes; there was one break, the duration of which was controlled by participants.

Tasks were presented in a fixed order, which is listed in Table 2, and included the following:

1. **Positive and Negative Affective States (PANAS) (Watson, Clark, & Tellegen, 1988)**. PANAS questionnaires were distributed on paper. Participants rated the degree to which certain adjectives described how they felt at time of questionnaire administration. Scores for each of these adjectives were then combined into scores for positive and negative affect.
2. **Stanford Sleepiness Scale (Hoddes, Zarcone, Smythe, Phillips, & Dement, 1973)**. Participants assessed their level of sleepiness on a 7-point scale (1 = Feeling active, vital, alert, or wide awake; 7 = No longer fighting sleep, sleep onset soon; having dream-like thoughts). Higher scores indicated more sleepiness.
3. **Alpha Attenuation Task (Stampi, Stone, & Michimori, 1995)**. This three-minute task involved alternating 30-second periods of eyes open and eyes closed, with a five-second rest between each period to eliminate artifact caused by opening and closing the eyes. This task assessed EEG frequencies associated with varying levels of sleepiness or alertness. The alpha attenuation coefficient (AAC) represents the ratio of eyes closed to eyes open. Alpha-theta ratios for eyes open and eyes closed conditions were also calculated. These analyses were conducted for low, high, and total alpha. Lower ratios have been associated with sleep deprivation, and thus represent greater sleepiness. Absolute theta, alpha, beta, and gamma power for eyes open and eyes closed conditions were also assessed. In general, lower alpha and higher theta when the eyes are closed indicate sleepiness, while higher beta and gamma represent alertness.

Table 2

Performance Assessment Battery Tasks and Timing

Task	Duration of Task
Positive and Negative Affect Scale (PANAS) * on paper	3 min
Stanford Sleepiness Scale	3 min
Alpha Attenuation Task	4 min
N-Back Working Memory Task	8 min
Break	As needed
Auditory Reaction Time Task	7 min
Novel P3 Task	10 min
Visual Reaction Time Task	8 min
Stanford Sleepiness Scale	3 min
Perception of Performance Scale	3 min
Total Approximate Time	**45 min**

4. **2-back Memory Task (Gevins & Cutillo, 1993).** During three blocks of 60 randomly presented letters, i.e., 180 stimuli presented within each session, participants were to identify target letters by pressing the "0" on the keyboard. Target letters were those that occurred in a series where the letter on the screen matched the one seen two trials before it, e.g., "**a**," "R," "**a**". The interstimulus interval was fixed at 2000 ms. Participants were to respond as quickly and accurately as possible. Analyses on accuracy data were conducted for target and non-target stimuli, and analyses on reaction time (RT) data were conducted only for target stimuli.
5. **Reaction Time Task.** Participants responded as quickly as possible to auditory tones (1000 Hz, 65 dB, 100 ms) presented binaurally by pressing the "0" on the keyboard. The interstimulus interval varied at random from 2000 to 10000 ms, and the total task lasted 6 minutes. Analyses were conducted for mean RT, RT standard deviation, the average of the 10% fastest RTs, the reciprocal of the average of the 10 % slowest (1/10% slowest) RTs, and the number of lapses (RTs $\geq$ 500 ms).
6. **Novel P3 Task**. Participants were presented with a series of auditory tones. At rare and random times, the standard 1000 Hz tone was replaced with a 2000 Hz target stimulus or a novel environmental sound. During each battery, 260 tones were presented. Standard stimuli were presented on 80% of trials; target tones and novel sounds were each presented on 10% of trials. One hundred novel stimuli were accessed from the public domain (available from http://cepl.nyspi.org/Resources/ Auditory_Stimuli/ auditory_stimuli.html); stimulus parameters are described in Fabiani, Kazmerski, Cycowicz, and Friedman (1996). Five additional tonal sounds were created in the Brock University Sleep Research Laboratory and matched to the

other novel stimuli for duration and intensity. Tones were delivered binaurally (average intensity = 77 dB; average duration = 330 ms; inter-stimulus interval = 1300 – 1700 ms). The participants were instructed that they would hear frequent, standard tones and rare, target tones and that these would be interspersed with odd, novel sounds. Their task was to respond as quickly and accurately as possible to the rare, target tones by pressing "0" on the keyboard. Analyses on accuracy were conducted for all stimulus types, while RT analyses were conducted for target stimuli only.

7. **Visual Reaction Time Task.** Participants responded as quickly as possible to visual stimuli ("X") presented in one of four quadrants of the screen, by pressing a corresponding key on the keypad ("1" – bottom left, "4" – top left, "3" – bottom right, "6" – top right). Stimuli were presented for 50 ms, followed by a blank screen for a maximum of 700 ms, during which a response was allowable; a response terminated this window. This sequence was followed by an intertrial interval of 700 ms, i.e., from response offset to onset of next stimulus. The task was divided into two blocks, each lasting three minutes. Analyses were conducted for accuracy and reaction time to errors.
8. **Subjective Performance Scale.** Participants assessed their performance, considering together all tasks in the previous battery, on a 5-point scale (1 = Very poor; 5 = Very good).

Event-related potential tasks. Event-related potential (ERP) tasks were administered to participants on the stimulus delivery night only. Tasks were programmed and delivered using STIM software (Compumedics Neuroscan Inc.). During a pitch oddball paradigm, participants were presented with a series of auditory tones. At rare and

random times, the standard 1000 Hz tone was replaced with a 2000 Hz target stimulus. Four hundred tones were presented in total. Standard stimuli were presented on 80% of trials; target tones were presented on 20% of trials. Tones were delivered binaurally via insert earphones (70 dB, 50 ms, inter-stimulus interval = 1000 – 2000 ms). Participants' task was to respond as quickly and accurately as possible to the rare, target tones by pressing a hand-held button. Analyses on accuracy were conducted for both stimulus types, while RT analyses were conducted for target stimuli only.

Participants also completed a paired-click paradigm. Two 0.04 ms square-wave clicks were played binaurally at 95 dB SPL (note that "clicks" are low frequency and short duration and therefore are not disturbing to participants) with a constant inter-stimulus interval of 500 ms. An inter-trial interval was held constant at 10 s between each pair of clicks. Participants were instructed to listen to the clicks but not to respond. Procedures for the paired-click paradigm are discussed in White and Yee (1997) and Milner et al. (2009; see Appendix A).

Neuropsychological testing. Participants came to the laboratory for a third off-protocol session, where they completed a short battery of neuropsychological tests. These tests were geared to measure various aspects of attention, memory, and executive functioning, and included the following: Wechsler Adult Intelligence Scale-III (WAIS-III: Digit Span, Digit-Symbol Coding) (Wechsler, 1997), Auditory Consonant Trigrams (Stuss & Benson, 1986), California Verbal Learning Test-II (CVLT-II) (Delis, Kramer, Kaplan, & Ober, 2000), Delis-Kaplan Executive Functioning System (D-KEFS: Trail Making Test, Colour-Word Interference, Tower Test, Design Fluency) (Delis, Kaplan, & Kramer, 2001), and the Comprehensive Test of Nonverbal Intelligence (CTONI)

(Hammill, Pearson, & Widerholdt, 1996). Participants also completed the Brock Adaptive Functioning Questionnaire (BAFQ; Dywan & Segalowitz, 1999) to assess functioning in their day-to-day lives, and the Spot-the-Word component of the Speed and Capacity of Language Processing Test (SCOLP) (Baddeley, Emslie, & Nimmo-Smith, 1993) as an estimate of premorbid I.Q.

Electrophysiological Recording and Analysis

During the screening night, polysomnographic data were collected in the Brock University Sleep Research Laboratory. Grass gold plated electrodes were applied to cleaned and exfoliated skin with conductive paste. Abdominal and thoracic respiration signals were collected during the screening night with respiration bands. During the screening night, electrodes to measure electroencephalography (EEG) were placed at C3 and C4; FPz acted as the recording reference and AFz as the ground. Electrooculography (EOG) was recorded with electrodes placed 1 cm from the outer canthus of either eye. EEG and EOG data were re-referenced offline to the contralateral mastoid. Electromyography (EMG) was recorded with a submental bipolar channel and bipolar channels recorded from each leg. Electrocardiography (EKG) was recorded via a bipolar channel with leads placed under each clavical. Finally, respiration was monitored with respiration bands placed across the chest and abdomen.

Data were sampled at 256 Hz using 64-channel Mizar Digital amplifiers on Sandman Elite software (Tyco, Inc.). A 60 Hz notch filter was applied to all channels. EKG and respiration channels had no other filters applied. A 0.1 Hz filter was applied to leg EMG channels; a 0.1 Hz and a 70 Hz filter were applied to EEG and EOG channels; and, a 0.1 Hz and 100 Hz filter were applied to submental EMG channels. Recordings

from the screening night were checked for sleep disorders, but were not scored for all-night sleep architecture.

On all three protocol nights, a 20-channel montage (FP1, FP2, F7, F3, Fz, F4, F8, FCz, T7, C3, Cz, C4, T8, P7, P3, Pz, P4, P8, O1, O2) (Pivik et al., 1993) was used to record EEG signals during each protocol night. Data were sampled at 250 Hz on Nights 1 and 2, and at 1000 Hz on Night 3, using 64-channel SynAmps2 amplifiers on Neuroscan software (Compumedics Neuroscan Inc.). No hardware or software filters were applied during recording. Nights were stage scored with a modified version of Rechtschaffen and Kales (1968) criteria; stage changes were marked at the precise moment of their occurrence, as opposed to the end of each 30 s epoch. This scoring technique ensures each stimulus is binned into the correct sleep stage. Sleep architecture variables were calculated for each night.

Phasic events were visually counted. Spontaneous K-complexes were visually identified at Fz in Stage 2 sleep on both recording nights. K-complexes were at least 0.5 s in duration; an amplitude criterion of 75 μV was used as a guide. While K-complexes are generated in slow wave sleep, slow, large amplitude delta waves in the background EEG make it difficult to reliably identify K-complexes in this stage. Density (number of K-complexes per minute of Stage 2 sleep) was calculated; as well, the mean inter-K-complex interval and interval standard deviation were calculated as measures of rhythmicity. To identify sleep spindles, Cz and Pz channels were specially filtered to display only frequencies between 12 and 16 Hz. Spindles were counted and duration measured at Cz in Stage 2, 3, and 4 on all three nights. Sleep spindles were required to be 0.5 s in duration, and to have a fusiform shape. Density (number of spindles per minute

of sleep), mean duration, and duration standard deviation were calculated; as well, mean inter-spindle interval and interval standard deviation were calculated as measures of rhythmicity.

Evoked K-complexes were measured in Stage 2 sleep on the stimulus delivery night to oddball target stimuli. EEG data were divided offline into trials ("sweeps"). Each sweep began 100 ms prior to stimulus onset and continued until 1900 ms after stimulus presentation. Data were manually inspected to reject trials that were composed of movement or electrical artifact. The average number of trials per participant is indicated in Appendix I. The N550 component was identified in the grand average waveforms at Fz, where it was maximal in the grand averages. N550 amplitude and latency were measured at all 20 recording sites for individual participants relative to prestimulus baseline EEG. Data were filtered at 30 Hz for display.

Prior to quantitative EEG or ERP analyses, data were inspected for movement and electrical artifact. Sections of data containing artifact were removed from analyses. EEG data were re-referenced offline to an average of A1 and A2. Power spectral analysis (PSA) was performed on EEG data recorded during the nights, using Fast-Fourier Transform analysis (FFT) techniques. EEG data were quantified as the absolute power (μV^2/Hz) of each of the following pre-defined frequency bands: slow wave, < 1 Hz; delta, 1-4 Hz; theta, 4–8 Hz; low alpha, 8–10 Hz; high alpha, 10–12 Hz; low sigma, 12–14 Hz; high sigma, 14-16 Hz; beta, 16-35 Hz; low gamma, 35–45 Hz; high gamma, 65-75 Hz. Sleep-scored data from each night were submitted to PSA according to stage, in 2-second periods. Stage 2 on the recording nights was divided into early and late Stage 2 (23:00 h to 03:00 h, 03:00 h to 07:00 h); the night was simply divided at the halfway

point based on clock time. A 75% overlap with hanning windowing was used. Power values were calculated at all 20 recording sites.

Waking data were analyzed in a similar manner. PSA was performed on EEG data recorded during the alpha attenuation task, using FFT techniques. EEG data were quantified as the absolute power ($\mu V^2/Hz$) of each of the following pre-defined frequency bands: delta, 0.5-4 Hz; theta, 4-8 Hz; low alpha, 8-10 Hz; high alpha, 10-12 Hz; total alpha, 8-12 Hz; sigma, 12-16 Hz; beta, 16-35 Hz; low gamma, 35-45 Hz; mid-gamma, 55-65 Hz; high gamma, 65-75 Hz. Data were submitted to PSA separately for eyes open and eyes closed sections of the data, in 2-second periods. A 75% overlap with hanning windowing was used. Power values were calculated at all 20 recording sites. The slow wave frequency band is only observable in sleep and therefore was not recorded in wakefulness. As well, while the sigma band was divided into low and high bands in sleep to reflect interest in the sleep spindle, the gamma band was more finely divided in wakefulness to allow examination of high frequency activity thought to represent alert wakefulness.

ERP analyses were conducted on EEG recorded during the oddball and paired-click paradigms. EEG data were divided offline into trials ("sweeps"). Each sweep began 100 ms prior to stimulus onset and continued until 900 ms after stimulus presentation. In wakefulness, eye blinks were regressed out of the data using a mathematical algorithm. In all states, data were manually inspected to reject trials that were composed of movement or electrical artifact. Trials were averaged separately for each stimulus type. The average number of trials per participant is indicated in Appendix I. The amplitudes and latencies of each component were measured at all 20 recording sites for individual participants

relative to prestimulus baseline EEG. When a component could not be visually identified, the amplitude was measured at the latency value from the respective grand average.

For the oddball paradigm, ERPs were measured in pre- and post-sleep wakefulness, Stage 2, slow wave sleep (SWS), and rapid eye movement (REM) sleep. In the grand average waveforms, N1 and P2 were identified at Cz, and the P300 was identified at Pz, where they were maximal. Data were filtered at 30 Hz for display.

For the paired-click paradigm, ERPs were measured in pre- and post-sleep wakefulness, Stage 2, and REM sleep. First, the N1 component was identified at Cz in the grand average waveforms, with a 0-30 Hz filter applied. This was used as a guide to locate the P50 component in the grand averages. The P50 component was identified at Cz with a 10-50 Hz filter applied, with the sweep time truncated to 0-200 ms. Data from 0-200 ms were filtered at 10-50 Hz for both measurement and display. See White and Yee (1997) and Milner et al. (2009; Appendix A) for description of analysis procedures.

Waking ERP analyses were conducted on EEG recorded during the Novel P3 oddball, n-back working memory, and visual reaction time tasks during each of the four performance assessments (pre- and post-sleep on Night 1 and Night 2). In the grand average waveforms for the Novel P3 and n-back tasks, N1 and P2 were identified at Cz, and the P300 was identified at Pz, where they were maximal. For the Novel P3 task, the novel P3 component was identified at Fz. Data were filtered at 30 Hz for display. For the visual reaction time task, error trials were averaged for each session, and then collapsed across the four recording sessions to form one overall average. In the grand average waveforms, the error-related negativity (ERN) and error positivity (Pe) were identified at

FCz, where they were maximal. Data were filtered at 1-10 Hz for measurement and display of ERP averages.

Procedure

Participants were recruited at the university and in the surrounding community. Advertisements announced that participants were being recruited for a study on sleep physiology and waking performance in both individuals who had sustained a TBI and non-injured good sleepers. Interested participants contacted the Sleep Research Laboratory for a telephone interview. Eligible participants visited the laboratory for an orientation session and screening night. Off-protocol, participants also completed a neuropsychological test battery. Following these screening procedures, participants spent three consecutive nights in the laboratory. The first two protocol nights were considered "recording nights", while the final night was considered a "stimulus delivery night". Procedures on the recording nights were nearly identical, while the stimulus delivery night involved separate procedures. Participants were invited to discuss the study with the researcher following the final night. They were provided with a $125 honorarium for their participation. Procedures are described below and illustrated in Figure 1.

EEG recording nights. Participants arrived at 19:30 h on the first night, to allow them time to practice performance tests a final time. On the second night, participants arrived at 20:00 h. A 20-channel electrode montage was applied with individual electrodes (electrode caps, while convenient, are neither comfortable nor reliable during overnight recordings). Participants completed the 45-min performance assessment battery beginning at 21:00 h. They were instructed to keep their eyes focused on a fixation point on the screen and to minimize blinking and movement. Following the battery,

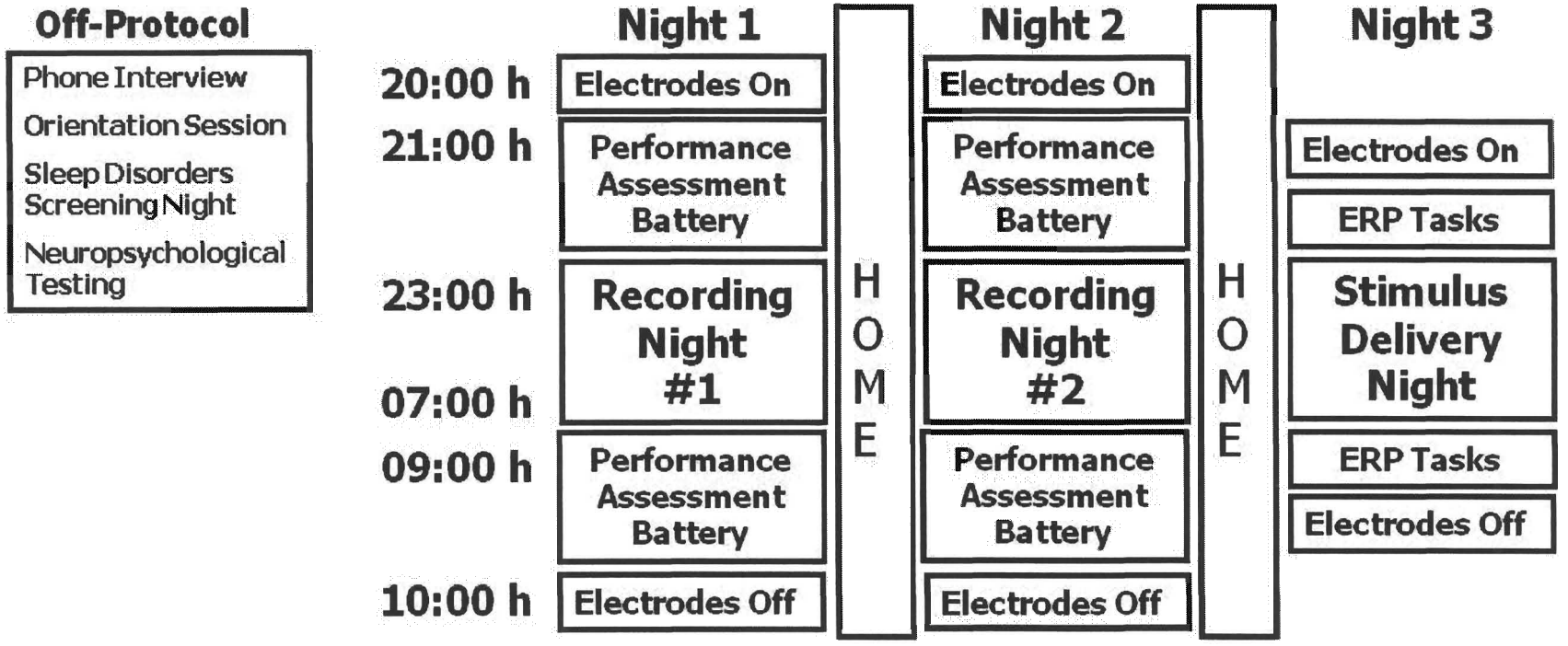


Figure 1. Schematic of the study protocol.

participants prepared for bed and completed a pre-sleep questionnaire, which included measures of subjective sleepiness, fatigue, and mood, and inquired about time that participants awoke that day, daytime napping, and alcohol, caffeine, and medication usage. Lights off occurred at 23:00 h. Sleep was recorded throughout the night. Lights on occurred at 07:00 h. Upon awakening, participants completed a post-sleep questionnaire, which contained the same subjective rating scales, and inquired about the quality and quantity of the previous night's sleep. Participants were provided with breakfast and given free time until 09:00 h. They then completed the same performance assessment battery that was given in the evening. Following each night, participants were free to leave the laboratory for the daytime, with instructions to follow their usual habits with respect to caffeine consumption and daily activities, and to refrain from napping.

Stimulus delivery night. Participants arrived at 21:00 h. The same 20-channel electrode montage was used. Participants completed a 10-minute paired-click paradigm and a 10-minute pitch oddball paradigm before bed. They were instructed to keep their eyes focused on a fixation point on the screen and to minimize blinking and movement. These were administered with lights on with participants seated at a computer workstation. The order of tasks was counterbalanced across participants. Following the tasks, participants prepared for bed and completed the pre-sleep questionnaire. Participants were also fitted with a pair of insert earphones to be worn throughout the night; these were secured to participants' ears with medical tape to ensure continuity of stimulus intensity. Lights off occurred at 23:00 h. Once participants achieved five minutes of consolidated Stage 2 sleep, stimulus delivery was initiated. Both the paired-click and pitch oddball paradigms were delivered in 10-minute blocks. The order of

stimulus presentation was randomized throughout the night. Participants were reminded that they could ask for stimulus delivery to be paused if they found stimuli disruptive, but no participants requested stimuli be paused. Thus, stimulus delivery continued uninterrupted through the night for each participant. Lights on occurred at 07:00 h. Upon awakening, participants completed the post-sleep questionnaire. Immediately following this, participants once again completed the paired-click and pitch oddball paradigms, with lights on and seated at a computer workstation.

Statistical Data Analysis

Data cleaning. Boxplots and Kolmorgorov-Smirnov tests were used to assess the normality of the data. EEG data were log transformed to eliminate the skewness inherent in the data. Data were also analyzed for outliers. While some participants had extreme scores on some variables, all data were judged to be plausible, and were therefore included in data analysis. For EEG and ERP measures, data from certain electrode sites for certain participants were missing due to technical problems, e.g., poor connection between the electrode and scalp. These missing data were resolved by using a "nearest neighbours" approach, where the missing data were replaced with values averaged from the nearest electrode sites.

Missing data. With respect to sleep data, there were no missing data for sleep architecture or spontaneous K-complex analyses. One TBI participant and one control participant each did not accrue any Stage 4 sleep on Night 3. Since these two participants were age-matched to each other, one matched pair was not included in analyses for Night 3 Stage 4 sleep spindle counting, quantitative EEG analysis in Stage 4, or oddball ERP analysis in slow wave sleep. In addition, one TBI participant, and thus also her age-

matched control, were removed from oddball and paired-click ERP analyses in Stage 2, slow wave sleep, and REM sleep on Night 3 because her earphones did not remain in her ears reliably through the night. One control participant, and thus also the age-matched TBI participant, were removed from all oddball ERP analyses on Night 3 due to a technical problem, where oddball stimuli were not marked in the EEG recordings, and thus ERP analyses could not be time-locked to stimuli.

With respect to waking data, there were no missing data for neuropsychological, behavioural, or quantitative EEG data. There were some points of missing data for subjective analyses where participants neglected to complete certain questions on various measures. Whereas there were no missing data for Novel P3 or n-back ERP analyses, there were only 15 matched pairs available for averaging for the visual reaction time task; the other 5 matched pairs did not have enough trials available for averaging.

Analytic strategy. Given that control and TBI participants were matched by age, within-subjects analyses were used to compare groups on measures of sleep architecture, phasic events, FFT, and ERPs, as well as waking subjective, behavioural, FFT, ERP, and neuropsychological waking data (N. DeCourville, personal communication, November 25, 2009; Howell, 1992). Specifically, paired samples t-tests were used to investigate group differences. For topographical data, Group (control, TBI) by Anterior/Posterior (frontal, central/temporal, parietal) by Medial/Lateral (left ventral, left dorsal, midline, right dorsal, right ventral) analyses of variance (ANOVAs) were used as a conservative approach to investigate group differences across the scalp. Significant three-way interactions were followed with Group by Medial/Lateral ANOVAs at each level of the Anterior/Posterior factor, while significant two-way interactions were followed with

group comparisons at each level of the topographic factor. Significant interactions from this level of analysis were then followed with paired samples t-tests to investigate group differences at each relevant electrode site. Group main effects from the original ANOVA were also reported. These procedures have been described by Dien and Santuzzi (2005), who described the use of repeated measures analysis of variance strategies when analyzing data from multiple electrode arrays.

Bivariate correlation analyses were run to examine the relationship between the continuous injury severity score and all dependent variables. Given that participants were recruited across a continuous range of injury severity, it was important to evaluate the effect that this potential moderating variable had on the data. In addition, examination of the TBI participants after all participants were recruited showed that most TBI participants could be grouped into one of two subgroups based on sleep complaint. Specifically, TBIs were grouped as either TBIs with complaints of insomnia (n=10) or TBIs with daytime fatigue (n=6); four TBI participants fell into neither category. Thus, a secondary analysis of the data based on this variable was planned, and is reported in instances where an overall group difference did not emerge. Paired t-tests to compare groups were run for each of the two subgroups separately. For topographic analyses, Group (TBI, control) by Anterior/Posterior (frontal, central, parietal) by Medial/Lateral (left lateral, left medial, midline, right medial, right lateral) ANOVAs were run to compare groups; ANOVAs were also run for each subgroup separately. Significant effects were followed up in the same way that was described above for overall group effects.

One-tailed tests were run in a post-hoc fashion to investigate uni-directional hypotheses when initial results generally supported hypotheses but were not statistically robust. This was true for all sleep architecture variables, K-complex variables, and delta EEG power in all stages of sleep. Two-tailed tests were used in all other circumstances. In all cases, violations to homogeneity of variance were addressed by applying the Greenhouse-Geisser correction. For simplicity, however, unadjusted degrees of freedom are presented throughout.

Finally, bivariate correlations were run between measures collected during sleep and wakefulness. Specifically, for TBIs and controls separately, correlation analyses were run to investigate the relationship between sleep architecture variables on all three protocol nights and subjective, behavioural, EEG, and ERP variables post-sleep on each respective night. The relationships between K-complex density in Stage 2 sleep on Nights 1 and 2 and behavioural, subjective, ERP, and EEG variables were also investigated. Similarly, the relationships between spindle density and spindle duration in all non-REM stages on all three nights and behavioural, subjective, ERP, and EEG post-sleep variables were examined. For ERP and EEG data, site Cz was chosen to investigate relationships with waking function. Each variable was investigated in the particular sleep stage(s) that were expected to produce the most robust relationships. Delta power in Stage 4 sleep and gamma power in early Stage 2 sleep on Nights 1 and 2 were investigated in relation to post-sleep measures of behavioural, subjective, ERP, and EEG waking function. Finally, latency and amplitude of the P50 component recorded during REM and Stage 2 sleep was investigated in relation to behavioural, subjective, and ERP waking function measures on

Night 3. As well, event-related potentials recorded in REM and Stage 2 sleep in response to oddball target stimuli were investigated in relation to waking function variables.

Both significant results ($p<.05$) and trends ($p<.10$) are presented in each section for most variables. Trends at single electrode sites were not included. Due to the exploratory nature of analyses investigating relationships between sleep and waking function, only significant results ($p<.05$) were reported in that section. In general, group differences that were illustrated by significant effects were consistent with those illustrated by trends in the data, such that reporting trends was helpful to describe the overall pattern and nature of group differences. Results that seemed spurious in nature were described as such throughout the document, and not interpreted in the Discussion. Overall, this approach was taken because of the novelty of the research questions and the paucity of prior data, and to provide greater direction for future research given the relatively small sample size.

Chapter 6: Sleep-Related Electrophysiology

Sleep Architecture

In general, consistent with hypotheses, TBIs showed evidence of poorer sleep compared to their matched controls. See Table 3 for means and standard deviations for all variables. Given the uni-directional hypothesis that TBIs would have worse sleep, group comparisons were one-tailed. Specifically, on **Night 1**, TBIs took longer to fall asleep, $t(19)=-2.21$, $p=.02$. On **Night 2**, TBIs had fewer minutes of Stage 2 sleep, $t(19)=2.26$, $p=.02$, less total sleep time, $t(19)=1.99$, $p=.03$, lower sleep efficiency, $t(19)=1.87$, $p=.04$, and more movement, $t(19)=-1.84$, $p=.04$. The **night-to-night variability** (absolute value of the difference between values on Night 1 and Night 2) in sleep architecture was analyzed. TBIs ($M=40.62$, $SD=23.17$) had a larger night-to-night difference than controls ($M=22.82$, $SD=23.26$) in minutes of Stage 2 sleep, $t(19)=-3.35$, $p=.002$, and TBIs ($M=16.35$, $SD=17.15$) had a greater difference than controls ($M=7.87$, $SD=6.14$) in sleep onset latency, $t(19)=-1.99$, $p=.03$. On **Night 3**, TBIs moved more than the control group, $t(19)=-2.78$, $p=.01$, and had a longer sleep onset latency, $t(19)=-1.78$, $p=.05$.

In addition, it was expected that injury severity would be associated with the degree of sleep disturbance. Greater injury severity was associated with more minutes of Stage 1 sleep on Night 1, $r=.44$, $p=.05$, and a trend suggested that it was related to lower sleep efficiency on Night 2, $r=-.41$, $p=.08$. Both relationships support hypotheses that TBIs would show evidence of poorer sleep.

Despite these findings, a number of variables did not differ between groups. In order to understand these null findings, secondary descriptive analyses were used to examine the impact of type of sleep complaint on the data. These comparisons yielded no

Table 3

Indices of Sleep Architecture on Each Protocol Night for TBIs and Controls

		Night 1		Night 2		Night 3	
		TBIs	Controls	TBIs	Controls	TBIs	Controls
		n=20	*n*=20	*n*=20	*n*=20	*n*=20	*n*=20
Total Sleep Time (min)	*M*	402.16	406.89	404.19	418.74	381.07	391.23
	SD	38.82	47.20	25.87	34.70	50.83	38.59
Sleep Efficiency (%)	*M*	83.24	84.46	83.85	86.78	79.08	81.22
	SD	7.63	9.84	5.32	7.12	10.07	8.04
Sleep Onset Latency (min)	*M*	24.27	16.75	25.55	19.56	23.49	15.76
	SD	18.30	11.81	21.60	15.62	18.36	8.66
Wakefulness (min)	*M*	17.53	12.12	13.44	18.50	9.37	11.00
	SD	22.25	14.01	10.45	38.51	8.73	14.10
Stage 1 (min)	*M*	37.95	37.85	38.79	32.25	61.39	58.69
	SD	23.71	28.89	18.80	25.82	38.01	31.86
Stage 2 (min)	*M*	217.57	220.69	195.47	217.63	213.99	212.08
	SD	44.00	36.04	38.04	29.07	38.48	27.38
Stage 3 (min)	*M*	20.39	21.27	19.90	20.47	19.90	20.68
	SD	7.30	6.59	9.40	6.94	7.84	7.70
Stage 4 (min)	*M*	80.17	74.52	81.10	74.40	59.56	63.03
	SD	29.44	32.97	22.58	27.94	26.26	29.73
REM sleep (min)	*M*	84.04	90.41	107.72	106.23	87.62	95.44
	SD	27.78	27.49	26.93	24.96	18.29	20.98
Movement Time (min)	*M*	25.27	24.92	25.79	21.40	29.74	20.80
	SD	8.53	16.14	10.29	8.79	13.20	8.15
Wake After Sleep Onset (min)	*M*	7.09	6.76	4.24	10.47	4.23	6.52
	SD	14.65	13.49	8.25	37.98	7.91	14.25

Note. REM = rapid eye movement

significant group differences, although a trend suggested that TBIs with complaints of insomnia (M=42.18, SD=21.26) had more Stage 1, i.e., light sleep, on the first night than controls (M=30.67, SD=23.46), $t(9)$=-2.05, p=.07. In general, sleep architecture results confirmed expectations that TBIs would have poor sleep.

Sleep Phasic Events

Spontaneous K-complexes. K-complex density, i.e., number of K-complexes per minute, was calculated for Stage 2 on Nights 1 and 2. As well, the average interval between K-complexes was calculated as an index of periodicity. The standard deviation of this interval was calculated as a measure of variability. See Table 4a for overall means and standard deviations for all variables. Given that K-complexes were expected to be reduced and more variable for TBIs, group comparisons were one-tailed. Consistent with hypotheses, there was strong evidence that TBIs had disruptions to spontaneous K-complexes. With respect to **K-complex density**, TBIs had fewer K-complexes on both Night 1, $t(19)$=3.88, p=.001, and Night 2, $t(19)$=2.87, p=.01 (see Figure 2). Interestingly, an observation of the means showed that each sleep complaint subgroup had fewer K-complexes than their respective matched controls (see Table 4b for density means and standard deviations per sleep complaint subgroup). As well, TBIs had a larger **interval between K-complexes** on Night 1, $t(19)$=-2.57, p=.01, and Night 2, $t(19)$=-1.89, p=.04, indicating that K-complexes occurred further apart in time, consistent with the idea that there were fewer K-complexes per minute. TBIs also had a larger **interval standard deviation** on Night 1, $t(19)$=-2.51, p=.01, indicating more variability in K-complex periodicity. Although the variability in K-complexes within a single night was greater for

Table 4

Spontaneous K-complexes in Stage 2 on Each Recording Night for TBIs and Controls

(a) Variable		Overall Group Differences			
		Night 1		Night 2	
		TBIs	Controls	TBIs	Controls
		n=20	*n*=20	*n*=20	*n*=20
Density (#/min)	*M*	2.68	4.40	2.83	4.08
	SD	0.95	1.49	0.94	1.28
Inter-KC Interval (s)	*M*	17.97	12.92	17.57	13.81
	SD	6.55	4.06	6.83	4.38
Inter-KC Interval *SD*	*M*	26.19	18.36	25.62	20.51
	SD	10.59	7.41	11.41	7.74
		Group Differences for Density (#/min)			
		Night 1		Night 2	
(b) Subgroup		TBIs	Controls	TBIs	Controls
Insomnia	*n*	10	10	10	10
	M	2.95	4.82	2.93	4.05
	SD	1.10	1.81	1.05	1.35
Daytime Fatigue	*n*	6	6	6	6
	M	2.23	3.78	2.73	3.77
	SD	0.69	1.08	0.77	1.22
No Complaints	*n*	4	4	4	4
	M	2.68	4.27	2.72	4.63
	SD	0.84	1.01	1.11	1.34

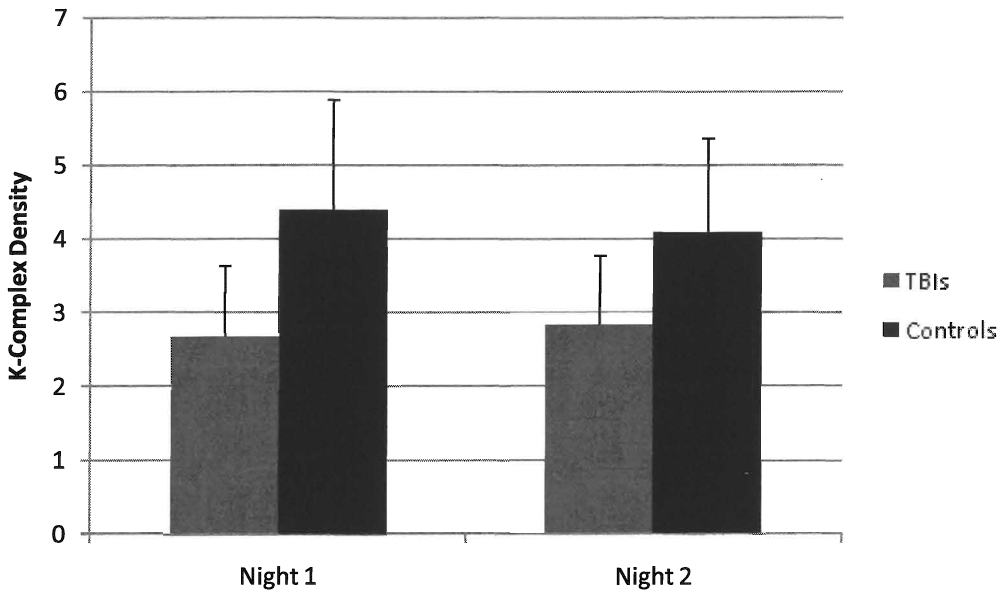


Figure 2. Mean K-complex density (#/min) for TBIs and controls on Night 1 and Night 2. Standard deviations are represented by the error bars on each column. Note that TBIs had fewer K-complexes on each night.

TBIs than controls, night-to-night variability did not differ. Secondary descriptive analyses suggested that TBIs with insomnia (M=0.47, SD=0.30) had less **night-to-night variability** in K-complex density than controls (M=1.18, SD=0.75), $t(9)$=2.54, p=.03, inconsistent with expectations that TBIs would have more night-to-night variability.

In sum, there was strong evidence that TBIs had fewer K-complexes in Stage 2 sleep on both recording nights. This finding suggests a breakdown in the generation of K-complexes in TBIs, and may represent a disruption in sleep-protective mechanisms. In addition to the group difference in K-complex density, there was also some evidence to suggest a breakdown in the rhythmicity of K-complex generation.

Evoked K-complexes. On Night 3, TBIs had fewer evoked K-complexes than controls, $t(17)$=2.61, p=.02, consistent with results for spontaneous K-complexes. As well, **K-complex latency and amplitude** were measured to target stimuli during the oddball paradigm in Stage 2 sleep at each of 20 electrode sites. Group (control, TBI) by Anterior/Posterior (frontal, central, parietal) by Medial/Lateral (left lateral, left medial, midline, right medial, right lateral) analyses of variance (ANOVAs) for K-complex latency and amplitude were non-significant; thus, further tests at individual electrode sites were not carried out. Grand average waveforms at each site were consistent with hypotheses, showing the N550 component to be smaller at frontocentral sites for TBIs (n=18) compared to controls (n=18). See Figure 3 for site Fz, where the K-complex was maximal. Thus, although strong evidence existed for differences in spontaneous K-complexes between groups, the paradigm used in this study did not produce statistically significant evidence to support differences in evoked K-complexes.

Sleep spindles. Sleep spindle density, i.e., number of sleep spindles per minute,

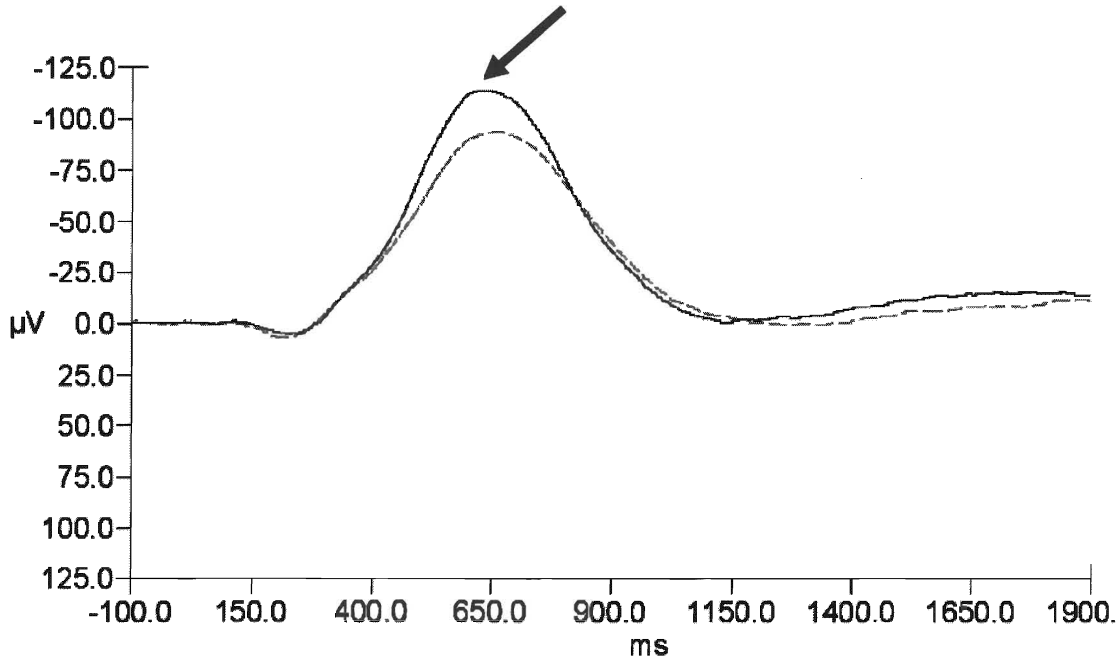


Figure 3. Grand average waveform of the evoked K-complex to oddball target stimuli in Stage 2 on Night 3, at site Fz. Solid black lines represent controls, and light grey dashed lines represent TBIs. Stimulus onset occurred at 0 ms; downward deflections are positive in polarity; data are filtered at 30 Hz. The arrow indicates the N550 component. Note that the N550 component appeared smaller in amplitude for TBIs.

was calculated for Stages 2, 3, and 4, on all three protocol nights. Average spindle duration was calculated to assess spindle length. The interval between sleep spindles was calculated as a measure of periodicity. As well, the standard deviations of both spindle duration and inter-spindle interval were calculated as measures of variability in spindle elicitation. See Table 5 for means and standard deviations for all variables. Given the equivocal nature of previous research, group comparisons for spindles were two-tailed.

With respect to **spindle density**, greater injury severity was associated with a lower spindle density in Stage 3 on Night 1, r=-.62, p=.004; a trend suggesting the same relationship was found in Stage 2 on Night 1, r=-.41, p=.07 (see Figure 4). In contrast, while no robust group differences were found, a trend suggested that TBIs had more spindles in Stage 4 on Night 2, $t(19)$=-1.97, p=.06. With respect to **spindle duration,** on Night 1, TBIs had longer spindles in Stage 3, $t(19)$=-2.44, p=.03, and a trend showed the same in Stage 4, $t(19)$=-2.03, p=.06 (see Figure 5). Spindle duration was expected to vary more in the TBI group than the controls, representing dysregulation in the generation of sleep spindles. While no robust statistical results were found, trends suggested that **spindle duration variability** was indeed greater for TBIs in Stage 4 on Night 1, $t(19)$=-1.94, p=.07, and in Stage 3 on Night 2, $t(19)$=-1.96, p=.07. As well, TBIs had a shorter **inter-spindle interval** in Stage 4 on Night 2, $t(19)$=2.11, p=.05; a trend showing that TBIs had a shorter interval in Stage 3 on Night 2 supported this result, $t(19)$=1.85, p=.08. In general, while correlation analyses supported the idea of a breakdown in spindle generation in TBIs, group comparisons suggested a potential compensatory mechanism, where TBIs had longer and more frequent sleep spindles.

The **night-to-night variability** in these measures was also assessed. TBIs

Table 5

Sleep Spindles in non-REM sleep on Each Protocol Night for TBIs and Controls

		Night 1		Night 2		Night 3	
		TBIs	Controls	TBIs	Controls	TBIs	Controls
Stage 2		*n*=20	*n*=20	*n*=20	*n*=20	*n*=20	*n*=20
Density (#/min)	*M*	9.51	10.19	9.45	10.07	8.75	9.62
	SD	1.03	2.69	1.75	2.60	3.37	2.87
Spindle Duration (s)	*M*	1.36	1.38	1.37	1.36	1.29	1.36
	SD	0.18	0.12	0.18	0.12	0.20	0.20
Spindle Duration *SD*	*M*	0.60	0.60	0.59	0.59	0.57	0.60
	SD	0.10	0.09	0.10	0.09	0.13	0.13
Inter-Spindle Interval (s)	*M*	4.14	4.28	4.29	4.33	4.59	4.55
	SD	0.79	1.30	1.14	1.31	1.65	1.72
Inter-Spindle Interval *SD*	*M*	5.18	5.00	6.17	5.12	5.12	4.96
	SD	1.30	1.29	5.11	1.44	2.07	2.13
Stage 3		*n*=20	*n*=20	*n*=20	*n*=20	*n*=20	*n*=20
Density (#/min)	*M*	9.85	9.83	10.58	9.83	10.56	10.59
	SD	2.52	2.84	2.80	3.38	3.46	3.61
Spindle Duration (s)	*M*	1.26	1.19	1.23	1.18	1.22	1.24
	SD	0.14	0.13	0.16	0.14	0.20	0.13
Spindle Duration *SD*	*M*	0.55	0.48	0.50	0.44	0.51	0.55
	SD	0.20	0.10	0.11	0.10	0.13	0.10
Inter-Spindle Interval (s)	*M*	3.92	4.85	3.88	5.08	3.86	4.01
	SD	1.64	2.50	1.80	2.73	1.61	1.59
Inter-Spindle Interval *SD*	*M*	3.88	4.73	3.83	4.84	3.94	3.81
	SD	1.88	2.81	2.30	2.82	2.67	1.82
Stage 4		*n*=20	*n*=20	*n*=20	*n*=20	*n*=19	*n*=19
Density (#/min)	*M*	8.69	8.61	9.68	8.35	9.67	8.59
	SD	2.96	3.01	2.42	2.91	2.47	3.06
Spindle Duration (s)	*M*	1.20	1.11	1.16	1.10	1.07	1.06
	SD	0.13	0.12	0.14	0.11	0.14	0.09
Spindle Duration *SD*	*M*	0.49	0.41	0.45	0.41	0.41	0.40
	SD	0.11	0.09	0.10	0.10	0.09	0.09
Inter-Spindle Interval (s)	*M*	5.30	6.25	5.01	6.70	5.13	6.38
	SD	2.35	3.08	1.85	3.54	2.07	3.09
Inter-Spindle Interval *SD*	*M*	5.42	6.35	5.23	6.74	5.16	6.62
	SD	2.72	3.46	2.17	3.70	2.37	3.51

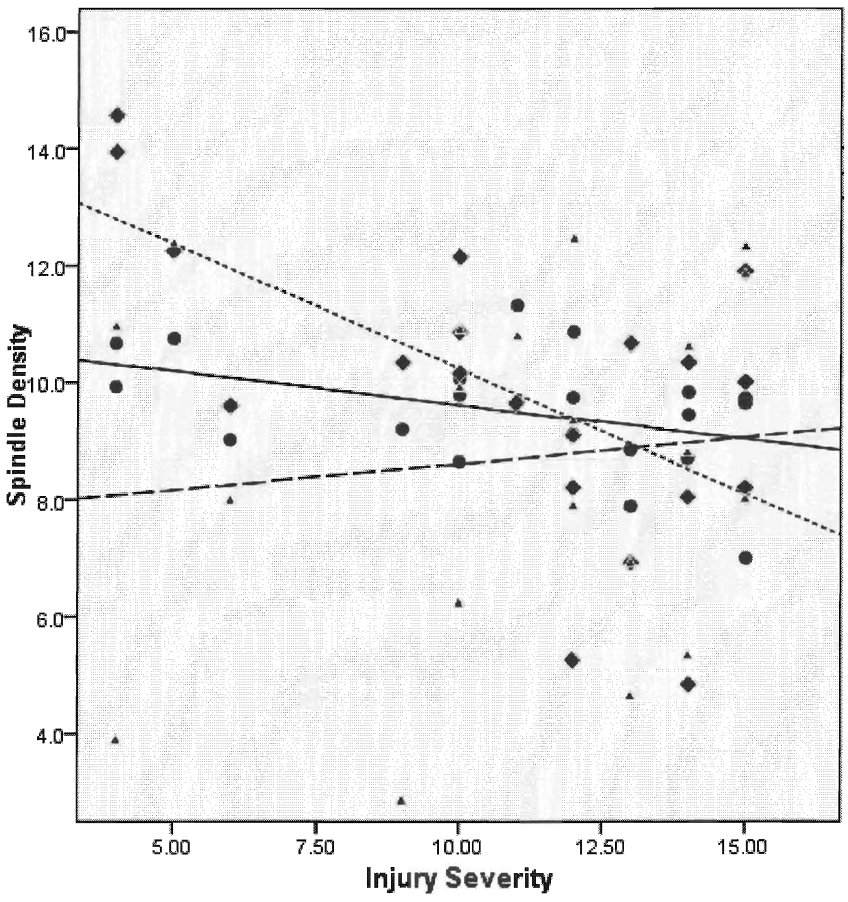


Figure 4. Relationship between injury severity and spindle density (#/min) for TBIs on Night 1 in Stage 2 (solid line, circles), Stage 3 (dotted line, diamonds), and Stage 4 (dashed line, triangles). A trend for Stage 2 and a significant effect for Stage 3 indicated that injury severity was negatively correlated with spindle density.

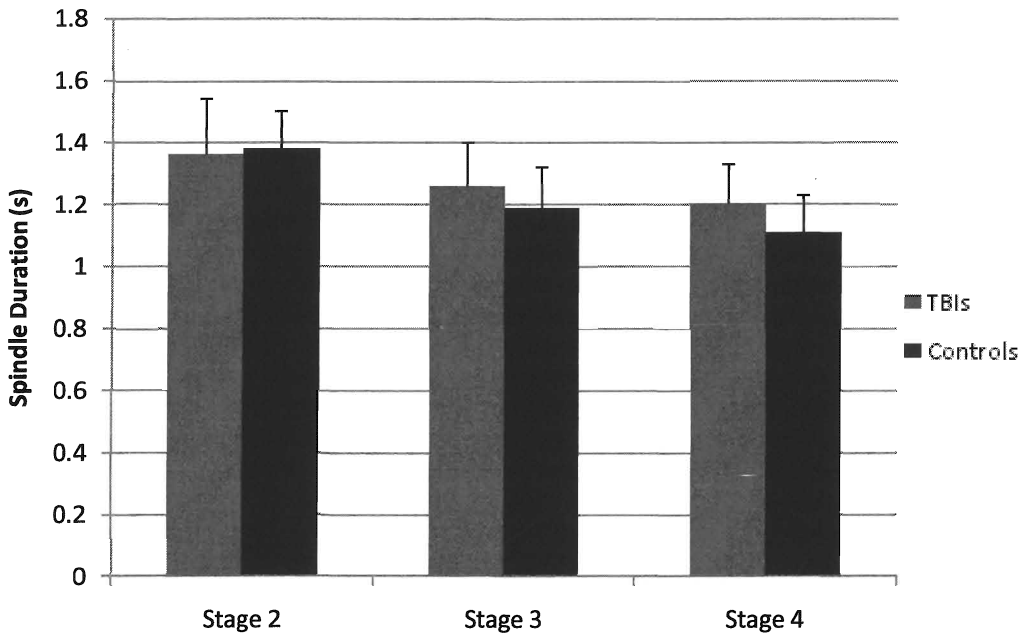


Figure 5. Mean spindle duration for TBIs and controls in all non-REM stages on Night 1. Standard deviations are represented by the error bars on each column. Note that TBIs had a longer spindle duration in Stages 3 and 4.

(M=1.72, SD=1.34) had more variability in Stage 3 spindle density than controls (M=0.96, SD=0.79), $t(19)$=-2.54, p=.02, and TBIs (M=0.09, SD=0.08) had more variability in Stage 3 spindle duration than controls (M=0.05, SD=0.04), $t(19)$=-3.62, p=.002. Greater injury severity was related to greater night-to-night variability in Stage 3 spindle density, r=.45, p=.05, inter-spindle interval, r=.52, p=.02, and inter-spindle interval standard deviation, r=.52, p=.02, confirming hypotheses that TBI severity was associated with dysregulation in sleep spindles. No group differences or relationships with injury severity were found for sleep spindles on the stimulus delivery night.

Quantitative Electroencephalography (qEEG)

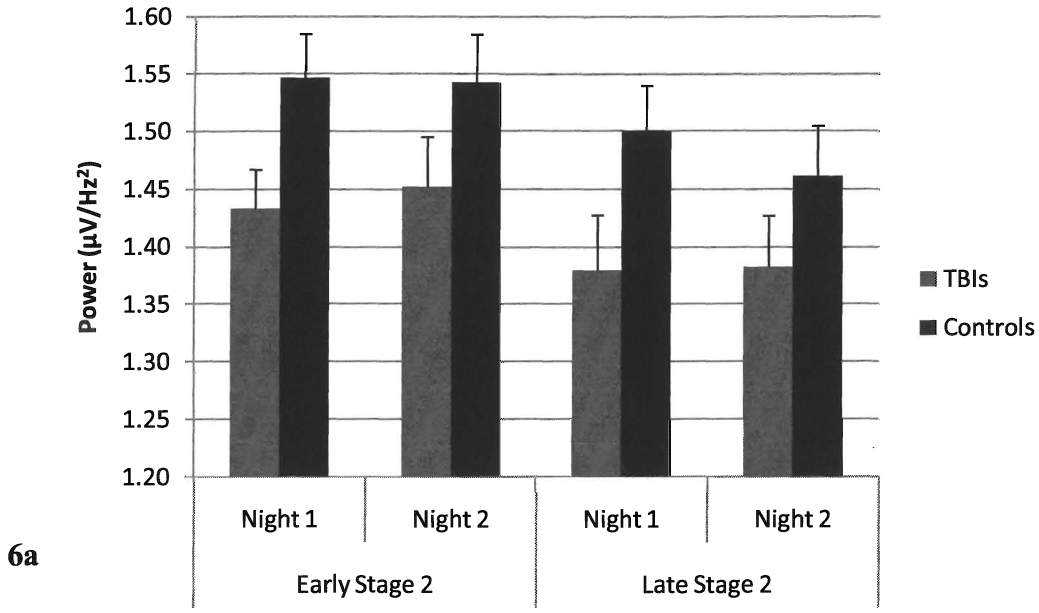
Power spectral analyses were computed on data in each sleep stage, on all three protocol nights. EEG data were decomposed into 10 frequency bands: slow wave (<1Hz), delta (1-4Hz), theta (4-8Hz), low alpha (8-10Hz), high alpha (10-12Hz), low sigma (12-14Hz), high sigma (14-16Hz), beta (16-25Hz), low gamma (35-45Hz), and high gamma (65-75Hz). Absolute power ($\mu V/Hz^2$) in each of these frequency bands was calculated at 20 electrode sites, then log transformed. Group (TBI, control) by Anterior/Posterior (frontal, central, parietal) by Medial/Lateral (left lateral, left medial, midline, right medial, right lateral) ANOVAs were run to investigate group differences in EEG power across the scalp. Both group main effects illustrating overall differences between TBIs and controls, and topographic interactions are presented below. In all stages, because delta power was expected to be lower for the TBI group overall, one-tailed tests were run to examine group main effects. Paired t-tests at each electrode site that followed group by topography interactions were two-tailed. Although beta and gamma were expected to be

higher for TBIs, two-tailed tests were run because it was thought that these results might be moderated by sleep complaint type.

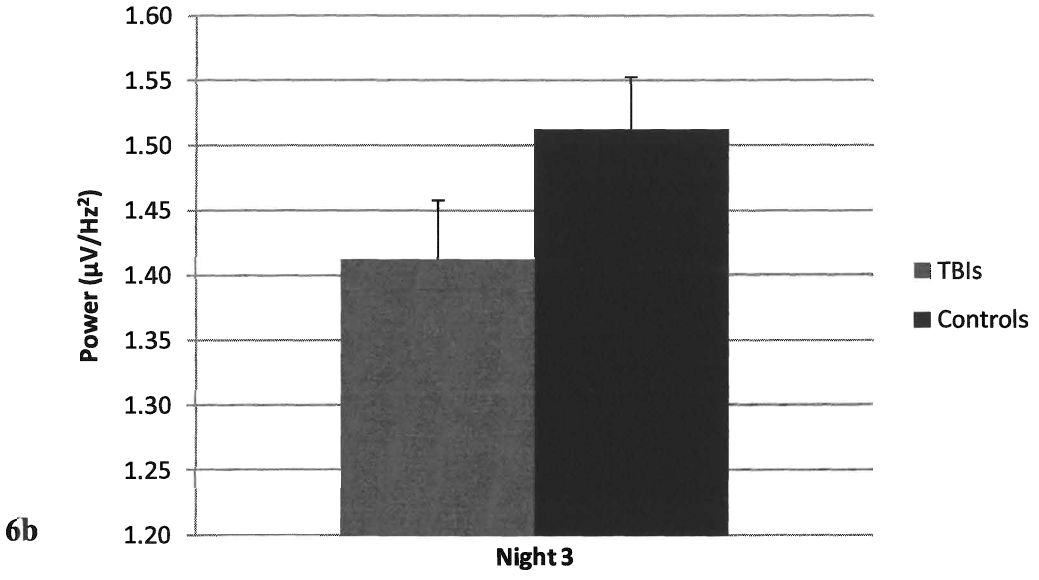
Stage 2. A number of group main effects were found for delta power. In early Stage 2, TBIs had less **delta power** than controls on Night 1, $F(1,19)=6.18$, $p=.01$, $\eta 2=.25$, and Night 2, $F(1,19)=4.34$, $p=.03$, $\eta 2=.19$. In late Stage 2 on Night 1, TBIs also had less delta power, $F(1,19)=5.54$, $p=.02$, $\eta 2=.23$ (see Figure 6a for Nights 1 and 2). In Stage 2 on Night 3, TBIs also had less delta power than controls, $F(1,19)=3.99$, $p=.03$, $\eta 2=.17$ (see Figure 6b).

In late Stage 2 on Night 2, group main effects showed that TBIs had more **beta power**, $F(1,19)=4.89$, $p=.04$, $\eta 2=.21$, and more **low gamma power**, $F(1,19)=8.68$, $p=.01$, $\eta 2=.31$ (see Figure 7a). As well, a Group by Anterior/Posterior interaction was found for **high gamma power** in late Stage 2 on Night 2, $F(2,38)=5.15$, $p=.01$, $\eta 2=.21$. A group difference was found at the parietal region, $F(1,19)=7.50$, $p=.01$, $\eta 2=.28$. Follow-up paired t-tests showed that TBIs had more gamma power at parietal sites (P7, P3, Pz, P4), *p*s=.004-.07 (see Figure 7b).

It was expected that injury severity would be related to EEG power. Greater injury severity was associated with less **low gamma power** in late Stage 2 on Night 1 at a number of scalp sites (FP1, F7, F8, T7, C3, Cz, C4, P7, P3, Pz, P4, P8, O1, O2), *p*s=.01-.10. In late Stage 2 on Night 2, a trend showed that greater injury severity was associated with less low gamma power at P7, $p=.06$. On Night 3, greater injury severity was associated with less low gamma power in Stage 2 at many sites (FP1, FP2, Fz, FCz, C3, T8, P7, P3, Pz, P4, P8, O1, O2), *p*s=.01-.10. Greater injury severity was associated with less **high gamma power** in late Stage 2 on Night 1 at multiple sites across the scalp (FP1,



6a



6b

Figure 6. Group main effects in log transformed delta (1-4 Hz) power ($\mu V/Hz^2$) showing that TBIs had less delta power than controls: (a) in early and late Stage 2 on each recording night; and, (b) in Stage 2 on Night 3. Standard errors are represented by the error bars on each column.

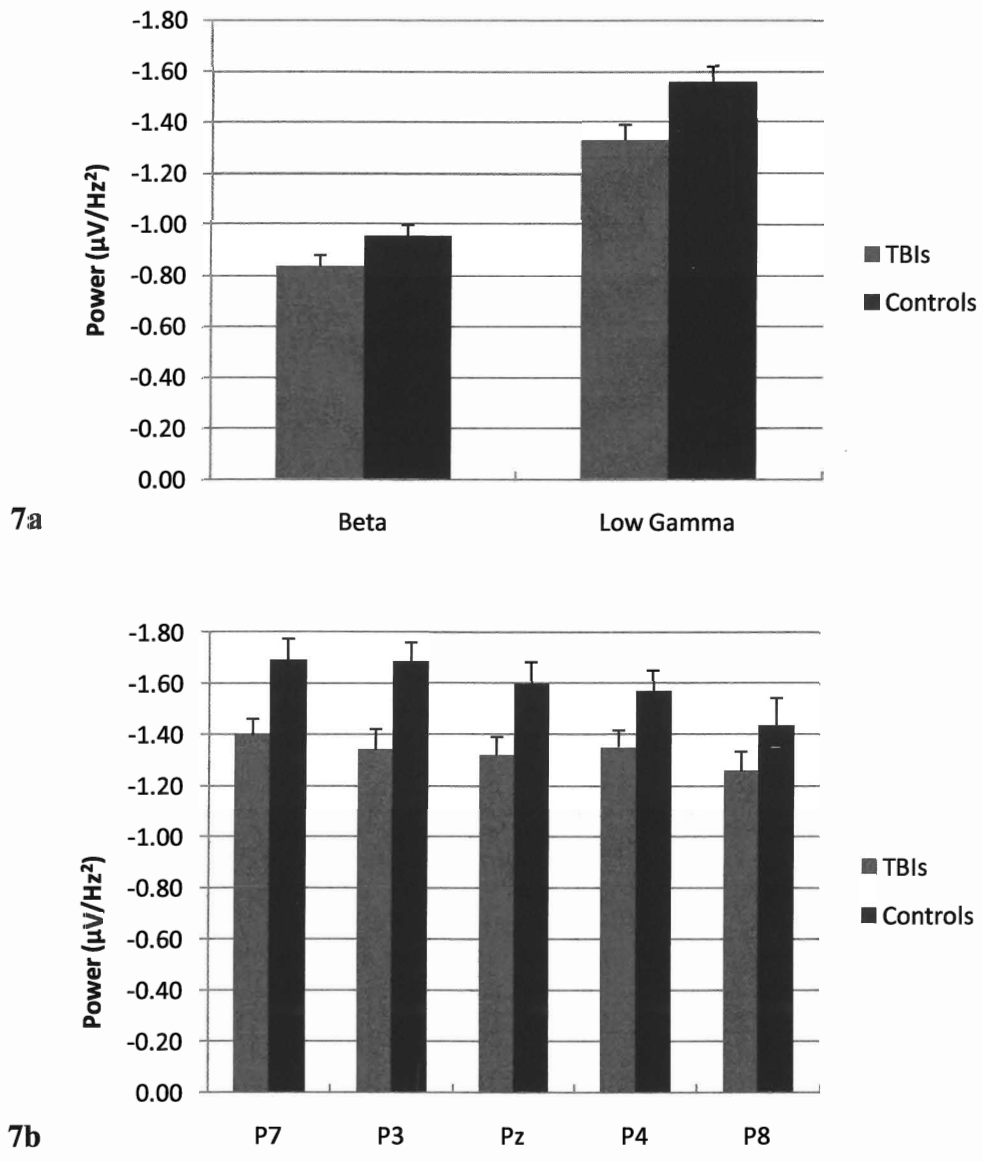


Figure 7. Mean log transformed power ($\mu V/Hz^2$) for TBIs and controls in late Stage 2 on Night 2; (a) group main effects for beta (16-25 Hz) and low gamma (35-45 Hz) power; (b) for high gamma (65-75 Hz) power at parietal sites. Standard errors are represented by the error bars on each column. Negative values closer to zero represent greater power. Note that TBIs had greater beta and gamma power.

FP2, F7, F3, F8, FCz, Cz, C4, T8, P7, P3, Pz, O1, O2), *p*s=.002-.09, and in Stage 2 on Night 3 at multiple sites (FP1, FP2, Fz, FCz, C3, Cz, P7, P3, Pz, P4, P8, O1, O2), *p*s=.02-.10. The fact that less severe injuries were associated with greater gamma power suggests that hyperarousal may be found primarily in milder injuries.

Although robust effects were found for delta, beta, and gamma power, no group differences were found for any other frequency band. Secondary analyses to understand the data for the insomnia and fatigue subgroups produced two effects. First, a trend toward a group main effect showed that TBIs with insomnia had less **slow wave power** than controls in Stage 2 on Night 3, $F(1,9)=3.85$, $p=.08$, $\eta 2=.30$. Second, a Group by Medial/Lateral interaction was found for the insomnia group for **high sigma power** in early Stage 2 on Night 2, $F(4,36)=3.40$, $p=.02$, $\eta 2=.27$. This interaction was followed by a trend suggesting a group difference along the right medial axis, $F(1,9)=3.77$, $p=.08$, $\eta 2=.30$. Paired t-tests at sites along this axis suggested that TBIs with insomnia had more sigma power than their counterparts at C4, $p=.06$, and P4, $p=.05$. While less slow wave power is consistent with the notion of impairments in sleep/wake regulation, the increase in sigma power, which may be related to increases in spindle activity in the TBI group, is more difficult to explain. An increase in sigma power and/or in spindles may be a compensatory response to sleep/wake dysregulation.

Overall, EEG power in Stage 2 sleep showed that TBIs had impairments in sleep/wake regulation. This was evidenced by reductions in delta power robustly across all protocol nights. TBIs were also characterized by greater beta and gamma power, suggesting the presence of hyperarousal in this light stage of sleep.

Slow wave sleep. A group main effect showed that TBIs had less **delta power** than controls in Stage 3 on Night 1, $F(1,19)=6.82$, $p=.01$, $\eta 2=.26$. A Group by Medial/Lateral interaction was found for delta power in Stage 4 on Night 1, $F(4,76)=2.97$, $p=.05$, $\eta 2=.14$. Follow-up ANOVAs revealed a trend toward a group difference at left medial regions, $F(1,19)=3.27$, $p=.09$, $\eta 2=.15$, and significant group differences at midline, $F(1,19)=6.55$, $p=.02$, $\eta 2=.26$, and right medial regions, $F(1,19)=5.12$, $p=.04$, $\eta 2=.21$. Follow-up paired t-tests showed that TBIs had less delta power at most sites (Fz, C3, Cz, C4, P3, Pz, P4), $ps=.01$-$.06$. A group main effect also showed that TBIs had less delta power than controls in Stage 4 on Night 2, $F(1,19)=3.44$, $p=.04$, $\eta 2=.15$.

There were no robust group differences in **low gamma power**, but a trend suggested that TBIs had less power in Stage 4 on Night 2, $F(1,19)=3.39$, $p=.08$, $\eta 2=.15$. Greater injury severity was associated with less low gamma power in Stage 3 on Night 1 at temporoparietal sites (T7, P7, P3, P4), $ps=.03$-$.06$, and in Stage 4 on Night 2 at C4, P3, P4, and O1, $ps=.05$-$.10$. In Stage 3 on Night 3, greater injury severity was associated with less low gamma power at most sites (FP1, FP2, F7, F3, Fz, FCz, C3, Cz, T8, P7, P3, Pz, P4, P8, O1, O2), $ps=.01$-$.09$. Again, less severe injuries were associated with the presence of hyperarousal.

Group main effects showed that **high gamma power** was lower for TBIs than controls on Night 1 in Stage 3, $F(1,19)=4.87$, $p=.04$, $\eta 2=.20$, and Stage 4, $F(1,19)=5.92$, $p=.03$, $\eta 2=.24$. In Stage 3 on Night 1, greater injury severity was associated with less high gamma power at F3, P7, O1, and O2, $ps=.02$-$.09$, and in Stage 4 on Night 1 at similar sites (FP1, F3, Cz, O1, O2), $ps=.04$-$.10$. In Stage 4 on Night 2, greater injury

severity was associated with less high gamma power at F7, p=.08, and O1, p=.03. In Stage 3 on Night 3, greater injury severity was associated with less high gamma power at multiple anterior and posterior sites (Fz, FCz, Cz, P7, P3, Pz, O1, O2), ps=.05-.08. Findings for low and high gamma were thus consistent with each other but in contrast to Stage 2. In slow wave sleep, TBIs had less gamma power and this was particularly true of those with more severe injuries. TBIs did, however, continue to show impairments in sleep regulation, reflected in lower delta power.

REM. On Night 2, greater injury severity was associated with less **slow wave power** at Fz, p=.05, and FCz, p=.03. On Night 1, a group main effect showed that TBIs had less **high gamma power** than controls, $F(1,19)=6.15$, p=.02, $\eta 2$=.25. No other group differences were found. Secondary descriptive analyses examining sleep complaint subgroup means were used to understand the nature of the data in this sleep stage. Two significant findings emerged. First, a Group by Anterior/Posterior by Medial/Lateral interaction for **high sigma power** on Night 2 suggested that TBIs with fatigue differed from their controls, $F(8,40)=3.39$, p=.01, $\eta 2$=.40. Follow-up tests yielded Group by Medial/Lateral interactions at frontal, $F(4,20)=3.90$, p=.02, $\eta 2$=.44, and parietal, $F(4,20)=2.50$, p=.08, $\eta 2$=.33, regions. Paired t-tests showed that TBIs with fatigue had more sigma power than controls at medial and midline frontal sites (F3, Fz, F4), ps=.04-.08, and at lateral and midline parietal sites (P7, Pz, P8), ps=.001-.06. Second, a Group by Anterior/Posterior by Medial/Lateral interaction for **beta power** on Night 2 suggested that TBIs with fatigue differed from controls, $F(8,40)=3.52$, p=.004, $\eta 2$=.41. Follow-up tests yielded a Group by Medial/Lateral interaction at the frontal region, $F(4,20)=8.29$, p<.001, $\eta 2$=.62, and group main effects at central, $F(1,5)=98.07$, p<.001, $\eta 2$=.94, and

parietal, $F(1,5)=57.28$, $p=.001$, $\eta 2=.92$, regions. Paired t-tests showed that TBIs with daytime fatigue had more beta power at all sites, $ps<.001$-$.05$. Thus, in general, TBIs with fatigue showed evidence of hyperarousal in REM sleep, reflected in higher beta activity, and also showed evidence of greater sigma power.

Summary. There were robust findings in Stage 2 sleep showing that TBIs had less delta power and greater beta and gamma power than their age-matched controls. Taken together, these results indicate that TBI was associated with a breakdown in sleep homeostatic mechanisms, and the presence of neurocognitive hyperarousal. The breakdown in sleep homeostasis was also witnessed in slow wave sleep. Hyperarousal in TBI may be most pronounced in periods of sleep that are inherently lighter, i.e., Stage 2 sleep, though hyperarousal was also evident in TBIs with daytime fatigue in REM sleep.

Event-Related Potentials (ERPs)

Oddball Paradigm. A pitch oddball paradigm was delivered in Stage 2 sleep (TBIs, $n=18$; controls, $n=18$), slow wave sleep (TBIs, $n=17$; controls, $n=17$), and REM sleep (TBIs, $n=18$; controls, $n=18$), as well as during pre- and post-sleep wakefulness (TBIs, $n=19$; controls, $n=19$) on the stimulus delivery night. In wakefulness, N1 and P2 were measured to standard and target stimuli, while the P300 component was measured only to target stimuli. During Stage 2 sleep, latency and amplitude of the N1, P2, N350, and P450 components were measured to standard and target stimuli. During slow wave sleep, N1 and P2 latency and amplitude were measured to both stimulus types. During REM sleep, latency and amplitude of the N1, P2, and N350 components were measured to both stimulus types. Components were measured at 20 electrode sites. Group (TBI, control) by Anterior/Posterior (frontal, central, parietal) by Medial/Lateral (left lateral,

left medial, midline, right medial, right lateral) ANOVAs were run to investigate group differences in ERPs across the scalp. Both group main effects illustrating overall differences between TBIs and controls, and topographic interactions are presented below. Two-tailed tests were used for all comparisons.

Wakefulness. Greater injury severity was associated with a longer **P300 latency** in pre-sleep wakefulness at Fz, FCz, C4, P7, and P8, *p*s=.03-.07, and in post-sleep wakefulness at T8, p=.04. A Group by Anterior/Posterior interaction was found for **P300 amplitude** in pre-sleep wakefulness, $F(2,36)=8.89$, p=.002, $\eta 2$=.33. A follow-up trend suggested a group difference at the frontal region, $F(1,18)=3.73$, p=.07, $\eta 2$=.17. Post hoc tests showed that TBIs had a larger P300 at F7, p=.05, and F3, p=.08. Greater injury severity was associated with a smaller P300 amplitude in post-sleep wakefulness at C4, P4, and P8, *p*s=.05-.08.

A secondary descriptive examination of the post-sleep subgroup means for P300 amplitude showed a trend toward a Group by Medial/Lateral interaction for the insomnia subgroup, $F(4,36)=3.32$, p=.06, $\eta 2$=.27, which was followed by group main effects at left lateral, $F(1,9)=7.46$, p=.02, $\eta 2$=.45, left medial, $F(1,9)=6.52$, p=.03, $\eta 2$=.42, midline, $F(1,9)=8.74$, p=.02, $\eta 2$=.49, and right medial regions, $F(1,9)=6.52$, p=.03, $\eta 2$=.42. Paired t-tests showed that TBIs with insomnia had a larger P300 amplitude than controls at most sites (F7, F3, Fz, F4, T7, C3, Cz, C4, P7, Pz), *p*s=.01-.07.

Few robust effects were found for the N1 component. A group main effect showed that **N1 latency** to standard stimuli in pre-sleep wakefulness was shorter for TBIs than controls, $F(1,18)=7.02$, p=.02, $\eta 2$=.28. Greater injury severity was associated with a shorter N1 latency to target stimuli in pre-sleep wakefulness at T7, p=.07, and to standard

stimuli in post-sleep wakefulness at T7, p=.01, and P7, p=.07. As well, a trend toward a Group by Medial/Lateral interaction was found for **N1 amplitude** to target stimuli in pre-sleep wakefulness, $F(4,72)=2.77$, p=.06, $\eta 2$=.13. Post hoc ANOVAs produced a trend suggesting a group difference at midline regions, $F(1,18)=3.82$, p=.07, $\eta 2$=.18. Post hoc t-tests showed that TBIs had a smaller amplitude at Cz, p=.06, and Pz, p=.03. Greater injury severity was associated with a larger N1 amplitude to target stimuli in pre-sleep wakefulness at P7, p=.03, and P3, p=.08, and in post-sleep wakefulness at P7, p=.05. No robust effects were found for the P2 component.

In sum, whereas correlation analyses suggested a longer latency and smaller amplitude for P300 for the more severe TBIs, overall group differences showed that the P300 was larger for TBIs compared to controls, particularly those with insomnia complaints. Whereas correlation evidence suggested a shorter latency and larger amplitude for N1 for the more severe TBIs, an overall group difference also showed that N1 was faster for TBIs compared to controls, but a trend suggested that N1 was smaller for TBIs compared to controls. In general, waking data suggested that TBIs and controls differed in information processing during pre- and post-sleep recording sessions.

Stage 2. A trend toward a group main effect suggested that **N1 latency** to standard stimuli in early Stage 2 was shorter for TBIs than controls, $F(1,17)=4.09$, p=.06, $\eta 2$=.19. For standard stimuli in late Stage 2, a Group by Anterior/Posterior interaction was found for N1 latency, $F(2,34)=4.35$, p=.04, $\eta 2$=.20. Follow-up ANOVAs produced a trend toward a group difference at frontal regions, $F(1,17)=3.56$, p=.08, $\eta 2$=.17, and a significant group difference at central regions, $F(1,17)=4.52$, p=.05, $\eta 2$=.21. Post hoc t-tests showed that TBIs had a shorter latency at frontocentral sites (F3, Fz, C3, Cz),

*p*s=.03-.07. Greater injury severity was related to a longer N1 latency in late Stage 2 at P8 to standard stimuli, *p*=.05, and target stimuli, *p*=.02, and to a larger **N1 amplitude** to target stimuli in early Stage 2 at P3, *p*=.03, and Pz, *p*=.01.

Greater injury severity was associated with a longer **P2 latency** to standard stimuli in late Stage 2 at FP1, F8, T7, and T8, *p*s=.06-.10. In early Stage 2, group main effects showed that **N350 latency** was shorter for TBIs to standard, $F(1,17)=5.09$, *p*=.04, $\eta 2=.23$, and target stimuli, $F(1,17)=8.64$, *p*=.01, $\eta 2=.34$. Greater injury severity was associated with a longer N350 latency to standard stimuli in late Stage 2 at C3, *p*=.06, and with a larger **N350 amplitude** to target stimuli in early Stage 2 at F8, *p*=.08, and T8, *p*=.01. Greater injury severity was associated with a shorter **P450 latency** to standard stimuli in early Stage 2 at FP1, *p*=.08, and FP2, *p*=.03, and to target stimuli in late Stage 2 at T7, *p*=.09.

Secondary descriptive analyses used to examine the impact of sleep complaint on the data showed unique results for N1 amplitude for the daytime fatigue group. There was a Group by Medial/Lateral interaction for standard stimuli in early Stage 2, $F(4,12)=6.32$, *p*=.01, $\eta 2=.68$, which was followed by trends toward group differences at midline, $F(1,3)=7.51$, *p*=.07, $\eta 2=.71$, and right lateral regions, $F(1,3)=6.90$, *p*=.08, $\eta 2=.70$. TBIs with fatigue had a smaller N1 amplitude at most relevant sites (Fz, F8, Cz, T8, P8), *p*s=.04-.10. A trend toward a group main effect for standard stimuli in late Stage 2 suggested that TBIs with fatigue had a smaller N1 amplitude overall, $F(1,3)=7.03$, *p*=.08, $\eta 2=.70$. A group main effect for target stimuli in early Stage 2 showed the same, $F(1,3)=19.91$, *p*=.02, $\eta 2=.87$. Finally, a Group by Medial/Lateral interaction for target stimuli in late Stage 2, $F(4,12)=13.70$, $p<.001$, $\eta 2=.82$, was followed by group

differences at left lateral, $F(1,3)=16.27$, $p=.03$, $\eta 2=.84$, left medial, $F(1,3)=14.54$, $p=.03$, $\eta 2=.83$, midline, $F(1,3)=16.46$, $p=.03$, $\eta 2=.85$, and right medial regions, $F(1,3)=18.34$, $p=.02$, $\eta 2=.86$. Paired t-tests showed that TBIs with fatigue had a smaller N1 amplitude at multiple scalp sites (Fz, F4, T7, C3, Cz, C4, P7, P3, Pz, P4), *p*s=.001-.09. While the main result from Stage 2 sleep was that N1 was smaller for TBIs with daytime fatigue, there was also some evidence that N1 latency was shorter for TBIs overall, and that information processing in this stage varied by injury severity.

Slow wave sleep. Greater injury severity was associated with a longer **N1 latency** to target stimuli primarily at frontocentral sites (FP2, Fz, F8, FCz, T7, C3, Cz, T8, Pz), *p*s=.04-.10, and with a larger **N1 amplitude** to standard stimuli at O1, $p<.001$, and O2, $p=.01$.

REM. In REM sleep, there were few results with respect to the N1 or P2 components. Greater injury severity was associated with a longer **N1 latency** to standard stimuli at T7, $p=.07$, and with a smaller **P2 amplitude** to standard stimuli at right hemisphere sites (F8, T8, P8), *p*s=.02-.05, and to target stimuli at F8, $p=.07$, and T8, $p=.05$. Greater injury severity was related to a longer **N350 latency** to standard stimuli at Pz, $p=.10$, and O2, $p=.06$, and to target stimuli at right hemisphere sites (F4, F8, P8, O2), *p*s=.02-.10. Greater injury severity was related to a smaller **N350 amplitude** to standard stimuli at P7, $p=.04$, and P3, $p=.04$, and to target stimuli at parietal sites (P7, P3, Pz), *p*s=.002-.07.

Secondary descriptive analyses used to examine the impact of sleep complaint on the data showed results for the N350 component. There was a Group by Anterior/Posterior interaction for the daytime fatigue group for N350 latency to target

stimuli, $F(2,6)=11.54$, $p=.01$, $\eta 2=.79$, which was followed by a trend toward a group difference at parietal sites, $F(1,3)=6.14$, $p=.09$, $\eta 2=.67$. TBIs with fatigue had a longer latency at most parietal sites (P3, Pz, P4, P8), $ps=.04$-$.08$. For N350 amplitude to standard stimuli, there was a trend toward a group main effect showing that TBIs with fatigue had a larger amplitude, $F(1,3)=39.68$, $p=.07$, $\eta 2=.16$.

In summary, greater injury severity was associated with reductions in P2 amplitude, suggesting impairments in inhibition. As well, greater injury severity was associated with a later and smaller N350, while TBIs with fatigue had a later but larger N350. These results were largely consistent with hypotheses that ERPs would show evidence of lighter sleep and impairments in inhibition for TBIs.

Summary. In wakefulness, correlation analyses suggested that greater injury severity was associated with slower and smaller P300s, consistent with previous reports of waking ERPs in TBI. Pre-sleep, there was some evidence that the P300 was larger frontally, and an examination of the subgroups post-sleep suggested that P300 was larger for TBIs with insomnia. Also in pre-sleep wakefulness, N1 to standard stimuli was faster for TBIs, while amplitude results were equivocal. These results suggested that information processing was faster and more extensive, showing that TBIs over-processed stimuli in wakefulness. Interestingly, group differences showed that N1 latency continued to be shorter for TBIs throughout Stage 2 sleep. This was true despite correlation evidence that greater injury severity was associated with a longer N1 latency in Stage 2 and slow wave sleep. Finally, there was evidence in REM sleep that greater injury severity was associated with slower and smaller N350 components, suggesting a breakdown in sleep regulation and consolidation. Overall, ERP results from the oddball

paradigm showed that TBIs had impairments in information processing and sleep regulation.

Paired-Click paradigm. A paired-click paradigm was run to elicit the P50 component as a measure of sensory gating. P50 was measured to the first and second click in a pair of stimuli; a suppression value (P50 amplitude to the second click relative to the first) was calculated to index sensory gating. The P50 is often difficult to identify due to its small amplitude; thus, the N1 component, which occurs shortly after the P50, was used as a guide to identify the P50 peak. Measurement of the N1 was also used as an index of early information encoding. Both the P50 and N1 were measured in pre- and post-sleep wakefulness (TBIs, n=20; controls, n=20), Stage 2 sleep (TBIs, n=19; controls, n=19), and REM sleep (TBIs, n=19; controls, n=19) on the stimulus delivery night (Night 3). The P50 was too difficult to measure reliably in slow wave sleep due to the low signal-to-noise ratio, i.e., small component relative to large amplitude background EEG. Components were measured at each of 20 electrode sites. Group (TBI, control) by Anterior/Posterior (frontal, central, parietal) by Medial/Lateral (left lateral, left medial, midline, right medial, right lateral) ANOVAs were run to investigate group differences in ERPs power across the scalp. Both group main effects illustrating overall differences between TBIs and controls, and topographic interactions are presented below.

In addition to these main statistical analyses, Group (control, TBI) by Stimulus (first, second) by Anterior/Posterior (frontal, central, parietal) by Medial/Lateral (left lateral, left medial, midline, right medial, right lateral) ANOVAs were used to investigate group differences in the change from first to second stimulus. Post hoc tests compared the two stimuli for each group separately. Two-tailed tests were used for all comparisons.

Wakefulness. In pre-sleep wakefulness, trends suggested that **P50 amplitude** to the second stimulus was larger for TBIs, $F(1,19)=3.57$, $p=.07$, $\eta 2=.16$ (see Figure 8 for the grand average waveforms showing the P50 component in pre- and post-sleep wakefulness). In post-sleep wakefulness, the **P50 suppression ratio** was larger for TBIs, $F(1,19)=3.60$, $p=.07$, $\eta 2=.16$. Greater injury severity was associated with a smaller P50 amplitude to the first stimulus in pre- sleep wakefulness at Fz, $p=.06$, and F8, $p=.02$, and in post-sleep wakefulness at F7, $p=.02$, and P4, $p=.09$. Greater injury severity was associated with a smaller suppression ratio pre-sleep at F7, $p=.06$, and C4, $p=.07$, and post-sleep at C3, $p=.08$; greater injury severity was associated with a larger post-sleep suppression ratio at FP2, $p=.06$. Greater injury severity was associated with a shorter **P50 latency** to the second stimulus in pre-sleep wakefulness at F3, Fz, C3, C4, P3, Pz, and O2, $ps=.002$-$.08$. In post-sleep wakefulness, greater injury severity was associated with a shorter P50 latency to the first stimulus at F7, F3, T7, C4, P7, P3, P4, P8, and O2, $ps=.001$-$.08$, and second stimulus at F3, C3, C4, T8, P7, P3, P4, P8, O1, and O2, $ps<.001$-$.07$.

Although amplitude results suggested poorer gating for TBI, no group differences were found for P50 latency. Secondary descriptive analyses in order to understand the data were run to compare each sleep complaint subgroup to their matched controls. For the daytime fatigue group, a Group by Anterior/Posterior by Medial/Lateral interaction, $F(8,40)=2.28$, $p=.04$, $\eta 2=.31$, was followed by a Group by Medial/Lateral interaction at the parietal region, $F(4,20)=3.00$, $p=.04$, $\eta 2=.38$. TBIs with fatigue had a shorter latency at Pz, $p=.05$. Other subgroup comparisons were not significant.

In pre-sleep wakefulness, there was a Group by Medial/Lateral interaction for **N1**

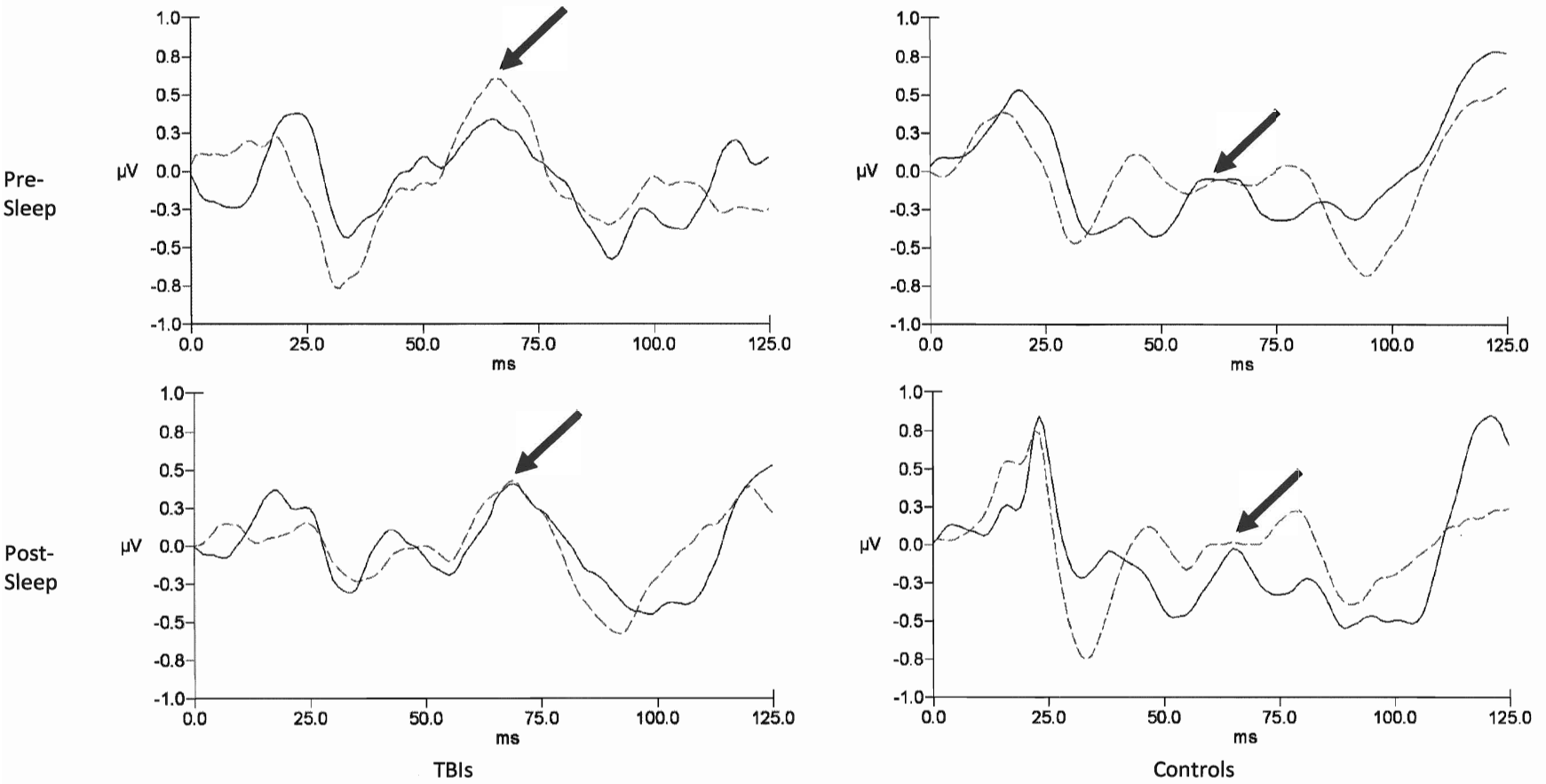


Figure 8. Grand average waveforms to paired-click stimuli in pre-sleep (top) and post-sleep (bottom) wakefulness on Night 3, at site Cz. TBIs' waveforms are shown on the left, and controls' on the right. Solid black lines represent waveforms evoked to the first stimulus, and light grey dashed lines represent those to the second stimulus. Stimulus onset occurred at 0 ms; downward deflections are negative in polarity; data are filtered at 10-50 Hz. The arrow indicates the P50 component. Note that the P50 component to the second stimulus is gated to a lesser extent for TBIs.

amplitude to the second stimulus, $F(4,76)=2.64$, $p=.04$, $\eta 2=.12$. Follow-up ANOVAs yielded trends toward group differences at left lateral, $F(1,19)=3.49$, $p=.08$, $\eta 2=.16$, and right lateral regions, $F(1,19)=3.52$, $p=.08$, $\eta 2=.16$. Post hoc paired t-tests suggested that TBIs had a larger amplitude at temporoparietal sites (T7, T8, P7, P8), $ps=.04$-$.08$. There was also a trend toward a group main effect suggesting that TBIs had a longer **N1 latency** to the first stimulus in pre-sleep wakefulness, $F(1,19)=3.57$, $p=.07$, $\eta 2=.16$.

In post-sleep wakefulness, there was a Group by Medial/Lateral interaction for N1 amplitude to the first stimulus, $F(4,76)=3.81$, $p=.03$, $\eta 2=.17$. Follow-up ANOVAs produced a trend toward a group difference at left lateral sites, $F(1,19)=4.19$, $p=.06$, $\eta 2=.18$, and significant group differences at left medial, $F(1,19)=6.06$, $p=.02$, $\eta 2=.24$, midline, $F(1,19)=7.34$, $p=.01$, $\eta 2=.28$, and right medial sites, $F(1,19)=6.13$, $p=.02$, $\eta 2=.24$. Post hoc paired t-tests showed that TBIs had a smaller N1 amplitude at multiple scalp sites (F7, Fz, F4, C3, Cz, C4, P7, P3, Pz), $ps=.01$-$.09$. A Group by Medial/Lateral interaction was also found for N1 amplitude to the second stimulus post-sleep, $F(4,76)=3.67$, $p=.04$, $\eta 2=.16$. A follow-up group difference was found along the right medial axis, $F(1,19)=4.27$, $p=.05$, $\eta 2=.18$. TBIs had a smaller N1 amplitude at C4, $p=.01$.

Greater injury severity was associated with a larger N1 amplitude in pre-sleep wakefulness to the first stimulus at C4, $p=.01$, and to the second stimulus at P3, $p=.03$, and in post-sleep wakefulness at F7, F4, and F8, $ps=.03$-$.08$. Greater injury severity was also associated with a larger **N1 suppression ratio** pre-sleep at P7, $p=.05$, and post-sleep at P4, $p=.04$. Greater injury severity was related to a shorter N1 latency to the first stimulus in pre-sleep wakefulness at P4, O1, and O2, $ps=.003$-$.06$.

ANOVAs run to investigate group differences in the **change in N1 amplitude** from the first to second stimulus revealed findings in line with hypotheses. Post-sleep, there was evidence of a Group by Stimulus by Medial/Lateral interaction, $F(4,76)=5.10$, $p=.02$, $\eta 2=.21$. Post hoc tests revealed a Stimulus by Medial/Lateral interaction for controls, $F(4,76)=3.74$, $p=.04$, $\eta 2=.17$. Follow-up ANOVAs yielded significant differences between stimuli at left lateral, $F(1,19)=7.21$, $p=.02$, $\eta 2=.28$, left medial, $F(1,19)=6.78$, $p=.02$, $\eta 2=.26$, and midline regions, $F(1,19)=7.85$, $p=.01$, $\eta 2=.29$, and produced a trend toward the same at right medial regions, $F(1,19)=3.29$, $p=.09$, $\eta 2=.15$. Paired t-tests to compare the first and second stimulus showed that N1 amplitude was smaller to the second stimulus than the first at most sites (F7, F3, Fz, T7, C3, Cz, C4, P7, P3, Pz, P4), $ps=.01$-$.07$. Post hoc tests found no differences between N1 amplitude to the first and second stimulus for TBIs. ANOVAs run to investigate group differences in the change in N1 latency from first to second stimulus produced a group main effect pre-sleep, $F(1,19)=5.88$, $p=.03$, $\eta 2=.24$, such that TBIs had a longer N1 latency overall.

In sum, results showed poorer gating for TBIs based on P50 amplitude and suppression ratio values. Greater injury severity was associated with faster stimulus processing, again demonstrating poor gating. N1 amplitude was also larger for TBIs pre-sleep, but N1 latency was longer; post-sleep, N1 was smaller and later. When N1 amplitude was compared between the first and second stimulus, controls only showed the expected gating. Overall, TBIs had impairments in sensory gating in wakefulness.

Stage 2. While there were no robust statistical results for P50 in Stage 2, trends toward group main effects suggested that **P50 amplitude** to the first stimulus was larger for TBIs, $F(1,18)=3.61$, $p=.07$, $\eta 2=.17$, but that **P50 latency** to the second stimulus was

longer for TBIs, $F(1,18)=3.41$, $p=.08$, $\eta 2=.16$. Greater injury severity was associated with a smaller P50 amplitude to the second stimulus at FP1, F7, F3, Fz, P3, and P8, *ps*=.03-.09. Greater injury severity was also associated with a smaller **suppression ratio** at FP1, F7, and C4, *ps*=.04-.07, but with a larger ratio at C3, P3, and Pz, *ps*=.05-.08. ANOVAs run to investigate group differences in the **change in P50 amplitude** from first to second stimulus produced a group main effect, $F(1,18)=6.49$, $p=.02$, $\eta 2=.27$, such that TBIs had a larger amplitude overall. ANOVAs run to investigate group differences in the **change in P50 latency** from first to second stimulus produced a Group by Stimulus interaction, $F(1,18)=5.72$, $p=.03$, $\eta 2=.24$. While there was no difference in P50 latency between stimuli for controls, a stimulus main effect showed that P50 latency was longer to the second stimulus compared to the first for TBIs, $F(1,18)=7.52$, $p=.01$, $\eta 2=.30$.

There were no robust group differences in the N1 component in Stage 2 sleep. However, a trend toward a group main effect suggested that **N1 amplitude** to the first stimulus was smaller in TBIs, $F(1,18)=3.21$, $p=.09$, $\eta 2=.15$. Greater injury severity was associated with a smaller N1 amplitude to the second stimulus at Fz, FCz, C3, Cz, C4, and P4, *ps*=.01-.05. Greater injury severity was associated with a larger **N1 suppression ratio** at F7, FCz, T8, and Pz, *ps*=.01-.09.

ANOVAs run to investigate group differences in the **change in N1 amplitude** from first to second stimulus produced a Group by Stimulus by Anterior/Posterior by Medial/Lateral interaction, $F(8,144)=3.11$, $p=.03$, $\eta 2=.15$. Post hoc tests revealed Stimulus by Anterior/Posterior by Medial/Lateral interactions for controls, $F(8,152)=2.80$, $p=.05$, $\eta 2=.13$, and for TBIs, $F(8,144)=3.10$, $p=.04$, $\eta 2=.15$. For controls, follow-up ANOVAs were non-significant. For TBIs, there was a stimulus main effect for

the difference between stimuli at frontal sites, $F(1,18)=12.31$, $p=.003$, $\eta 2=.41$, and Stimulus by Medial/Lateral interactions for central, $F(4,72)=3.86$, $p=.04$, $\eta 2=.18$, and parietal regions, $F(4,72)=3.18$, $p=.04$, $\eta 2=.15$. Surprisingly, N1 amplitude was smaller to the second stimulus compared to the first at all sites for TBIs, $ps=.001$-$.06$.

In summary, although TBIs had a larger P50 to the first stimulus, there was no other evidence of group differences in gating in Stage 2 sleep. Results for N1 amplitude showed the opposite, that TBIs had a smaller amplitude to the first stimulus. As well, for TBIs, N1 amplitude was smaller to the second stimulus compared to the first. These results suggest intact gating. In general, there were few group differences in sensory gating in Stage 2 sleep.

REM. Greater injury severity was related to a smaller **P50 amplitude** to the first stimulus at P3, $p=.08$, and to the second stimulus at C4, T8, P4, P8, $ps=.01$-$.08$. Greater injury severity was also related to a smaller **P50 suppression ratio** at F3, $p=.06$. There was also a trend toward a Group by Anterior/Posterior by Medial/Lateral interaction for **P50 latency** to the first stimulus, $F(8,144)=1.95$, $p=.06$, $\eta 2=.10$. Post hoc ANOVAs produced Group by Medial/Lateral interactions at central, $F(4,72)=2.74$, $p=.04$, $\eta 2=.13$, and parietal regions, $F(4,72)=4.76$, $p=.01$, $\eta 2=.21$. Follow-up t-tests supported a shorter latency for TBIs at P7, $p=.01$, and P3, $p=.05$.

In addition, there was a trend toward a Group by Anterior/Posterior by Medial/Lateral interaction for **N1 latency** to the first stimulus, $F(8,144)=2.28$, $p=.06$, $\eta 2=.11$. Follow-up ANOVAs produced group differences at frontal regions, $F(1,18)=4.24$, $p=.05$, $\eta 2=.19$, and central regions, $F(1,18)=4.64$, $p=.05$, $\eta 2=.21$, and produced a Group by Medial/Lateral interaction at parietal sites, $F(4,72)=3.02$, $p=.02$,

$\eta 2$=.14. Post hoc tests confirmed that TBIs had shorter N1 latencies at multiple scalp sites (F7, F3, Fz, F8, T7, C3, Cz, P3, Pz, P4), *p*s=.03-.10. Greater injury severity was related to a larger **N1 amplitude** to the second stimulus at P7, P3, and Pz, *p*s=.004-.08, and smaller **N1 suppression ratio** at P7, P8, and O2, *p*s=.04-.06. ANOVAs run to investigate group differences in the **change in N1 latency** from first to second stimulus produced a trend toward a group main effect, $F(1,18)=3.57$, $p=.08$, $\eta 2=.17$, such that TBIs had a shorter latency overall.

In sum, there were no group differences in P50 or N1 amplitude in REM sleep. Both P50 and N1 latency, however, were shorter for TBIs. While these results support the notion that TBIs processed stimuli faster than controls, there were no group differences in direct measures of sensory gating in REM sleep.

Summary. The grand average waveforms in wakefulness (Figure 8) clearly show that TBIs had poorer gating. This observation was supported by several statistical differences in wakefulness. In Stage 2, P50 to the first stimulus was larger for TBIs, but otherwise there were no indicators that they had impairments in sensory gating. Finally, in REM, P50 and N1 latency were shorter for TBIs, supporting the idea of impairments in stimulus processing for TBIs in sleep. In general, results showed that TBIs had impairments in sensory gating.

Chapter 7: Waking Performance, Subjective Ratings, and Electrophysiology

Neuropsychological Performance

Neuropsychological measures largely showed that TBIs were more impaired than controls across a number of domains of functioning. Given the uni-directional hypothesis that TBIs would perform more poorly, group comparisons were one-tailed. Importantly, there was no group difference between TBIs (M=46.80, SD=4.95) and controls (M=46.40, SD=7.03) on a word knowledge measure used to estimate **premorbid I.Q.,** $t(19)$=-0.19, p=.43. On a **trail-making task,** TBIs (M=16.95, SD=6.21) were slower than controls (M=13.90, SD=2.75) on a measure of visual scanning, $t(19)$=-1.94, p=.03, and TBIs (M=24.40, SD=15.93) were slower than controls (M=16.55, SD=8.03) on a measure of motor speed, $t(19)$=-1.89, p=.04. On a **list-learning task**, TBIs (M=6.75, SD=2.55) remembered fewer items than controls (M=8.15, SD=2.28) on the initial learning trial, $t(19)$=1.85, p=.04, and TBIs (M=6.00, SD=2.34) remembered fewer items than controls (M=7.90, SD=2.75) on the distractor trial, $t(19)$=2.00, p=.03. Secondary descriptive analyses produced one possibly spurious effect. TBIs with insomnia (M=8.50, SD=0.71) had better free recall than controls (M=7.80, SD=0.63) on a **digit-symbol coding task,** $t(9)$=-4.58, p=.001.

On a questionnaire measuring **day-to-day adaptive functioning,** TBIs were more impaired across a number of domains. TBIs had greater difficulty with excess caution, $t(19)$=-2.80, p=.01, planning, $t(19)$=-1.93, p=.04, attention, $t(19)$=-2.06, p=.03, impulsivity, $t(19)$=-1.98, p=.03, and social monitoring, $t(19)$=-1.83, p=.04. See Table 6 for means and standard deviations. Higher scores indicate more impairment. Secondary descriptive analyses of the data showed, not surprisingly, that TBIs with fatigue (M=15.00, SD=2.97) had more difficulty than controls (M=9.33, SD=3.20) with arousal,

Table 6

Indices of Adaptive Day-to-Day Functioning for TBIs and Controls

		TBIs n=20	Controls n=20
Planning	*M*	15.90	12.65
	SD	5.62	3.38
Initiation	*M*	8.80	7.95
	SD	3.25	3.35
Flexibility	*M*	9.40	8.10
	SD	2.85	2.17
Excess Caution	*M*	16.10	13.05
	SD	3.85	3.25
Attention	*M*	18.10	15.00
	SD	4.83	4.89
Memory	*M*	18.30	15.85
	SD	4.94	4.78
Arousal	*M*	11.55	10.10
	SD	3.69	3.19
Emotionality	*M*	9.25	8.65
	SD	2.02	2.83
Impulsivity	*M*	13.20	11.20
	SD	3.16	3.09
Aggression	*M*	9.75	8.45
	SD	3.70	2.87
Social Monitoring	*M*	15.80	13.60
	SD	3.22	2.91
Empathy	*M*	9.10	8.65
	SD	2.31	2.48

$t(5)=-2.77$, $p=.04$. TBIs with fatigue ($M=12.50$, $SD=4.72$) also had more difficulty than controls ($M=7.83$, $SD=1.94$) with aggression, $t(5)=-2.57$, $p=.05$. Overall, there was evidence for greater impairment for the TBI group in various domains, especially processing speed, working memory, and adaptive functioning.

Injury severity was correlated with a number of **neuropsychological measures**, showing that more severe injuries were associated with greater impairment. Greater injury severity was associated with a lower premorbid I.Q., $r=-.39$, $p=.09$, and with poorer analytic performance on the geometric categories subtest of a non-verbal test of intelligence, $r=-.43$, $p=.06$, suggesting that greater injury severity was associated with impairments in intellectual functioning in verbal and non-verbal domains. Greater injury severity was also associated with poorer performance on memory measures including the number of items recalled on multiple variables from a list-learning task: fifth learning trial, $r=-.38$, $p=.09$; total score, $r=-.39$, $p=.09$; distractor trial, $r=-.41$, $p=.07$; free recall after short, $r=-.49$, $p=.03$, and long delays, $r=-.48$, $p=.03$; and cued recall after short, $r=-.49$, $p=.03$, and long delays, $r=-.41$, $p=.08$; greater injury severity was also associated with fewer perseverative errors on the list-learning task, $r=-.40$, $p=.08$. Greater injury severity was related to poorer scores on a complex working memory test after short, $r=-.60$, $p=.01$, moderate, $r=-.53$, $p=.02$, and long delays, $r=-.62$, $p=.004$, as well as total score, $r=-.74$, $p<.001$. Greater injury severity was associated with fewer self-corrected errors on the word reading trial of an inhibition task, $r=-.45$, $p=.05$, but with more self-corrected errors on the interference trial of the same task, $r=.42$, $p=.07$. Greater injury severity was associated with poorer performance on the first trial of a digit span task that represents simple working memory capacity, $r=-.60$, $p=.01$, and on a second trial that

requires individuals to manipulate information in mind, r=-.61, p=.01; greater injury severity was also associated with a poorer total score on this task, r=-.71, p<.001. As well, greater injury severity was related to reduced design fluency on a simple fluency trial, r=-.41, p=.07, and a trial that involves switching between cognitive sets, r=-.39, p=.09. In general, these correlations demonstrate that greater injury severity was associated with poorer performance on measures of attention, memory, and executive functioning.

As well, there were a number of positive correlations between injury severity and degree of impairment in **adaptive functioning**. Specifically, greater injury severity was associated with greater difficulty in the following domains: planning, r=.44, p=.05, initiation, r=.45, p=.05, flexibility, r=.40, p=.08, excess caution, r=.53, p=.02, memory, r=.61, p=.01, arousal, r=.57, p=.01, impulsivity, r=.61, p=.004, and social monitoring, r=.43, p=.06. Again, greater injury severity was related to greater impairment.

In conclusion, neuropsychological data illustrated a number of impairments for TBIs. Specifically, there was evidence that they were slower, had poorer working memory, and reported difficulties with day-to-day adaptive functioning. In addition, there was robust evidence that greater injury severity was associated with poorer neuropsychological performance across multiple domains of functioning.

Mood, Sleepiness, and Perceived Sleep Quality

Measures of mood, sleepiness and participants' subjective reports of their sleep were collected pre- and post-sleep on each night. Given the hypothesis that TBIs would rate their sleep as poorer, comparisons for sleep quality variables were one-tailed; other comparisons were two-tailed. Table 7 shows mood rating means and standard deviations.

Table 7

Ratings of Mood Pre- and Post-Sleep on Each Protocol Night for TBIs and Controls

		Pre-Sleep Night 1		Post-Sleep Night 1		Pre-Sleep Night 2		Post-Sleep Night 2		Pre-Sleep Night 3		Post-Sleep Night 3	
		TBIs	Controls	TBIs	Controls	TBIs	Controls	TBIs	Controls	TBIs	Controls	TBIs	Controls
		n=20	*n*=20	*n*=20	*n*=20	*n*=20	*n*=20	*n*=20	*n*=20	*n*=20	*n*=20	*n*=20	*n*=20
Visual Analogue Scales													
Calm-Irritable	*M*	16.33	29.20	28.00	32.88	20.33	23.80	32.05	26.63	19.43	21.45	39.25	33.98
	SD	16.05	21.72	22.64	23.10	15.88	17.01	25.69	22.48	16.82	14.35	29.72	25.28
Happy-Sad	*M*	20.63	27.35	34.60	34.78	24.13	24.93	33.73	31.08	21.05	28.65	29.33	35.30
	SD	18.68	19.87	22.06	17.06	23.92	14.30	21.78	18.89	19.73	17.93	18.06	18.58
Energetic-Sluggish	*M*	62.98	61.23	58.50	56.93	56.05	51.18	67.30	56.85	59.15	54.78	63.93	63.43
	SD	25.96	23.48	25.86	19.44	20.62	21.99	24.35	18.69	28.24	19.33	24.61	22.59
Relaxed-Tense	*M*	16.00	24.63	23.20	31.85	19.15	24.40	25.40	31.15	17.98	25.98	25.43	34.03
	SD	14.52	21.25	21.34	21.31	18.40	18.85	24.51	21.90	17.25	19.00	20.61	26.83
PANAS													
Positive Affect	*M*	27.75	20.40	21.80	18.60	26.45	19.30	23.13	18.40				
	SD	9.65	6.01	7.06	6.48	9.47	7.12	8.56	5.37				
Negative Affect	*M*	11.80	11.45	11.35	10.75	10.90	10.70	11.00	10.35				
	SD	1.58	1.64	1.57	1.12	1.55	1.26	1.75	0.67				

On **visual analogue measures of mood** (calm- irritable; happy-sad; energetic-sluggish; relaxed-tense), only one difference emerged. TBIs were calmer than controls pre-sleep on Night 1, $t(19)=2.57$, $p=.02$. **Positive and negative affect** measured with the PANAS differed among groups. TBIs had more positive affect than controls pre-sleep on Night 1, $t(19)=-2.93$, $p=.01$, and pre-sleep on Night 2, $t(19)=-2.61$, $p=.02$. A trend also suggested that TBIs had more positive affect post-sleep on Night 2, $t(19)=-1.98$, $p=.06$. Greater injury severity was associated with less positive affect pre-sleep on Night 1, $r=-.48$, $p=.03$, and a trend suggested the same relationship pre-sleep on Night 2, $r=-.43$, $p=.06$. Overall, TBIs appeared to have better mood than controls, in contrast with expectations.

Paired-samples t-tests did not reveal any group differences in **sleepiness or fatigue** ratings from the pre- and post-sleep questionnaires. A trend showed that greater injury severity was related to greater sleepiness pre-sleep on Night 2, $r=.40$, $p=.08$, and a significant positive correlation showed the same relationship pre-sleep on Night 3, $r=.47$, $p=.04$. Greater injury severity was also associated with greater fatigue pre-sleep on Night 2, $r=.55$, $p=.01$, and pre-sleep on Night 3, $r=.52$, $p=.02$. A secondary descriptive analysis of the data showed a trend suggesting that TBIs with daytime fatigue ($M=4.75$, $SD=1.54$) were sleepier than controls ($M=3.00$, $SD=0.63$) pre-sleep on Night 2, $t(5)=-2.41$, $p=.06$. In general, TBIs with more severe injuries, and those with complaints of fatigue, reported greater sleepiness and fatigue.

Participants also rated their **sleepiness at the beginning and the end of the performance assessment battery**. Greater injury severity was associated with greater sleepiness pre-sleep on Night 1 at the beginning of the battery, $r=.52$, $p=.02$, and at the end, $r=.58$, $p=.01$, as well as pre-sleep on Night 2 at the beginning of the battery, $r=.68$,

p=.001. Whereas there were no group differences in these sleepiness ratings, a secondary descriptive analysis provided results for sleepiness ratings at the end of the battery that were consistent with expectations. A trend showed that TBIs with daytime fatigue (M=4.83, SD=1.72) rated themselves as sleepier than controls (M=3.50, SD=1.22) pre-sleep on Night 1, $t(5)$=-2.39, p=.06. A trend also suggested that TBIs with insomnia (M=3.70, SD=1.83) rated themselves as less sleepy than controls (M=4.50, SD=1.35) pre-sleep on Night 1, $t(9)$=1.92, p=.09. TBIs with insomnia (M=2.40, SD=0.97) rated themselves as less sleepy than controls (M=4.00, SD=1.56) pre-sleep on Night 2, $t(9)$=3.54, p=.01, and TBIs with insomnia (M=2.50, SD=0.85) rated themselves as less sleepy than controls (M=3.30, SD=1.16) post-sleep on Night 2, $t(9)$=2.75, p=.02. Again, TBIs with more severe injuries, and those with complaints of fatigue, reported greater sleepiness; TBIs with insomnia complaints reported less sleepiness. Finally, participants also **rated their performance** on the performance assessment battery. A trend suggested that TBIs (M=2.83, SD=0.72) rated their performance more poorly than controls (M=3.42, SD=0.90) pre-sleep on Night 1, $t(11)$=1.87, p=.09. Greater injury severity was associated with lower performance ratings post-sleep on Night 1, r=-.44, p=.05, and pre-sleep on Night 2, r=-.59, p=.03.

Participants also provided ratings of sleep quality. See Table 8 for means and standard deviations for sleep quality ratings. TBIs' higher scores on a **"best-worst" visual analogue scale** post-sleep on Night 2 indicated that they rated their sleep as poorer than controls, $t(19)$=-2.02, p=.02. There were no group differences for a **composite measure of sleep quality** that was calculated by summing participants' responses across a number of questions. However, an examination of the subgroup means revealed a weak

Table 8

Ratings of Sleep Quality Pre- and Post-Sleep on Each Protocol Night for TBIs and Controls

		Pre-Sleep Night 1		Post-Sleep Night 1		Pre-Sleep Night 2		Post-Sleep Night 2		Pre-Sleep Night 3		Post-Sleep Night 3	
		TBIs	Controls	TBIs	Controls	TBIs	Controls	TBIs	Controls	TBIs	Controls	TBIs	Controls
Best-Worst Scale	*n*	20	20	20	20	20	20	20	20	20	20	20	20
	M	44.93	38.55	47.88	45.88	50.83	48.33	46.35	33.45	43.53	37.85	52.05	49.88
	SD	20.33	15.85	18.78	13.82	19.58	17.41	20.61	17.87	20.56	19.13	20.42	19.66
Sleep Quality Composite	*n*	20	20	19	19	20	20	20	20	20	20	20	20
	M	34.76	34.19	39.48	38.45	39.34	39.30	38.57	35.64	35.77	37.19	39.79	41.92
	SD	12.78	10.62	13.96	11.25	12.28	11.60	11.87	12.82	13.11	11.93	11.54	12.65
Sleep Onset Latency (min)	*n*	19	19	20	20	18	18	18	18	18	18	18	18
	M	31.08	20.08	43.40	25.25	32.69	25.61	34.33	21.39	31.08	26.22	31.67	18.94
	SD	30.19	20.69	39.94	14.09	24.47	15.08	24.49	13.48	22.27	22.19	23.58	10.69
Total Sleep Time (hr)	*n*	20	20	20	20	20	20	20	20	19	19	19	19
	M	6.41	7.28	6.74	6.96	6.66	7.20	6.52	7.43	7.07	7.39	6.61	6.87
	SD	1.85	1.63	1.59	0.86	1.71	0.90	1.38	0.59	0.91	0.95	1.34	1.08
No. of Awaken-ings	*n*	18	18	19	19	18	18	19	19	18	18	18	18
	M	1.06	1.44	4.00	3.66	3.58	3.78	3.76	3.45	2.53	3.42	5.39	5.39
	SD	1.16	1.15	2.29	2.39	1.54	2.02	1.96	2.13	1.77	2.43	3.55	3.36

Note. Sample sizes are indicated for each variable. Data were missing when participants failed to complete questionnaire items.

trend suggesting that TBIs with insomnia (M=42.95, SD=9.74) provided higher, i.e., poorer, ratings than controls (M=34.61, SD=11.80) pre-sleep on Night 2, $t(9)$=-1.92, p=.09.

Specific measures of sleep quality (sleep onset latency, total sleep time, number of awakenings) suggested that TBIs rated their sleep more poorly than controls. TBIs rated themselves as having a longer **sleep onset latency** post-sleep on Night 1, $t(19)$=-2.15, p=.02, Night 2, $t(17)$=-1.96, p=.03, and Night 3, $t(17)$=-2.13, p=.02. TBIs also indicated that they had less **total sleep time** post-sleep on Night 2, $t(19)$=2.47, p=.01. There was also a trend suggesting that greater injury severity was associated with estimates of fewer **awakenings** post-sleep on Night 1, r=-.43, p=.07. On most variables, TBIs judged their sleep to be worse.

To further explore group differences in sleep quality ratings, secondary descriptive analyses were used to investigate the impact of sleep complaint. A weak trend suggested that TBIs with fatigue (M=49.17, SD=44.99) reported a longer sleep onset latency than controls (M=9.92, SD=5.83) pre-sleep on Night 1, $t(5)$=-2.13, p=.09, while TBIs with insomnia (M=43.88, SD=20.22) reported a significantly longer sleep onset latency than controls (M=23.13, SD=14.62) pre-sleep on Night 2, $t(7)$=-2.64, p=.03. Sleep complaint also moderated ratings of total sleep time. Specifically, TBIs with insomnia (M=5.85, SD=1.83) reported less sleep than controls (M=7.28, SD=0.55) post-sleep on Night 1, $t(9)$=2.51, p=.03, and TBIs with insomnia (M=5.75, SD=1.90) reported less sleep than controls (M=7.40, SD=0.53) pre-sleep on Night 2, $t(9)$=2.77, p=.02. TBIs with daytime fatigue (M=7.67, SD=0.52) reported more sleep than controls (M=6.50, SD=0.89) post-sleep on Night 1, $t(5)$=-4.18, p=.01.

In general, TBIs rated their sleep as worse than controls; this was particularly true of TBIs with insomnia. Sleepiness and fatigue measures confirmed subjective complaints of insomnia or daytime fatigue. There was also some evidence that TBIs with more severe injuries were sleepier than controls.

Reaction Time and Accuracy

On recording nights, groups were compared on accuracy and reaction time collected during the performance assessment battery. On Night 3, groups were compared on accuracy and reaction time recorded during the oddball task. All comparisons were two-tailed. For the **auditory reaction time task**, there were no group differences. A trend toward a positive correlation between injury severity and reaction time standard deviation pre-sleep on Night 2, r=.43, p=.06, suggested that greater injury severity was associated with more variable reaction times.

Greater injury severity was also associated with lower **N-back task accuracy** to standard stimuli pre-sleep on Night 1, r=-.44, p=.05, and post-sleep on Night 2, r=-.50, p=.03. A trend also suggested that greater injury severity was associated with lower **Novel P3 task accuracy** to novel stimuli pre-sleep on Night 2, r=-.43, p=.06, suggesting overall that greater injury severity was associated with poorer performance. Despite these relationships, a weak trend suggested that TBIs (M=207.95, SD=0.22) had better Novel P3 task accuracy than controls (M=207.60, SD=0.82) to standard stimuli post-sleep on Night 2, $t(19)$=-1.79, p=.09. A secondary descriptive analysis to explore the impact of sleep complaint on the data showed that TBIs with insomnia (M=26.00, SD=0.00) were more accurate than controls (M=25.20, SD=1.14) to Novel P3 target stimuli pre-sleep on Night 2, $t(9)$=-2.23, p=.05. As well, TBIs with insomnia (M=452.69, SD=73.74) had

faster **reaction times** than controls (M=549.94, SD=66.61) to Novel P3 target stimuli post-sleep on Night 1, $t(9)$=2.85, p=.02, and a trend suggested that TBIs with insomnia (M=444.23, SD=59.39) also had faster reaction times than controls (M=512.01, SD=50.69) to Novel P3 target stimuli pre-sleep on Night 2, $t(9)$=2.19, p=.06. Finally, there were no group differences for the **visual reaction time task, or oddball behavioural data**.

Overall, correlation analyses indicated that greater injury severity was associated with less accurate and more variable performance. There was also evidence that TBIs with insomnia had faster and more accurate stimulus processing on a novelty processing task.

Quantitative Electroencephalography (qEEG)

Power spectral analyses were computed on data collected during the alpha attenuation task to measure physiological arousal at four timepoints. Data were collected during alternating periods of eyes open and eyes closed. EEG data were decomposed into the following frequency bands: delta (0.5-4 Hz), theta (4-8 Hz), low alpha (8-10 Hz), high alpha (10-12 Hz), total alpha (8-12 Hz), sigma (12-16 Hz), beta (16-35 Hz), low gamma (35-45 Hz), mid-gamma (55-65 Hz), and high gamma (65-75 Hz). Absolute power ($\mu V/Hz^2$) in each frequency band was calculated at 20 electrode sites, then log transformed. Ratios of alpha power with eyes closed relative to eyes open and ratios of alpha to theta power were first computed on the original data. Lower values for both ratios represent greater sleepiness. Group (TBI, control) by Anterior/Posterior (frontal, central, parietal) by Medial/Lateral (left lateral, left medial, midline, right medial, right lateral) analyses of variance (ANOVAs) were run to investigate group differences in EEG

power across the scalp. Both group main effects illustrating overall differences between groups and topographic interactions are presented below. All comparisons were two-tailed.

Alpha attenuation coefficient (AAC). Ratios of alpha power with eyes closed to eyes open (alpha attenuation coefficient) were investigated as indices of sleepiness. Lower ratios indicate more sleepiness. There were no group differences, though injury severity was correlated with the AAC. Pre-sleep on Night 2, greater injury severity was associated with higher values, i.e., less sleepiness, for the **AAC for low alpha** at most scalp sites (FP1, FP2, F7, F3, Fz, F4, F8, FCz, T7, C3, Cz, C4, P3, Pz), *p*s=.04-.10, and for **total alpha** at FP1, FP2, and F8, *p*s=.04-.08. Greater injury severity, however, was associated with lower values for the **AAC for high alpha** post-sleep on Night 1 at O2, p=.05, and post-sleep on Night 2 at T7, p=.06. Overall, most evidence surprisingly suggested that TBIs with more severe injuries were less sleepy.

Alpha/theta ratio. Ratios of alpha power relative to theta power were investigated. Lower ratios indicate more sleepiness. While no group differences emerged, a secondary descriptive analysis of the data suggested that sleep complaint subgroups differed in sleepiness. Specifically, there was a Group by Anterior/Posterior interaction for the daytime fatigue group for the **high alpha/theta ratio** with eyes closed pre-sleep on Night 1, $F(2,10)=12.32$, p=.002, $\eta 2$=.71. This interaction was followed by a group difference at the parietal region, $F(1,5)=10.56$, p=.02, $\eta 2$=.68. Paired t-tests showed that TBIs with fatigue had a lower ratio, i.e., more sleepiness, at most parietal sites (P3, Pz, P4, P8), *p*s=.01-.08. There was a trend toward a Group by Anterior/Posterior interaction for the insomnia group for the high alpha/theta ratio with eyes closed pre-sleep on Night

2, $F(2,18)=3.76$, $p=.08$, $\eta 2=.30$. This interaction was followed by a trend toward a group difference at the parietal region, $F(1,9)=3.78$, $p=.08$, $\eta 2=.30$. Paired t-tests showed trends suggesting that TBIs with insomnia had a higher ratio, i.e., less sleepiness, at Pz, $p=.06$, and P8, $p=.09$. As well, a weak trend toward a group main effect for the **total alpha/theta ratio** with eyes closed post-sleep on Night 2 showed that TBIs with insomnia had less sleepiness than controls, $F(1,9)=3.51$, $p=.09$, $\eta 2=.28$.

Injury severity was correlated with many alpha/theta ratio measures. Trends showed that greater injury severity was associated with higher values, i.e., less sleepiness, for the **low alpha/theta ratio** with eyes closed pre-sleep on Night 1 at F7, T7, and O1, *p*s=.09; low alpha/theta ratio with eyes closed post-sleep on Night 1 at T7, $p=.06$; and, low alpha/theta ratio with eyes closed pre-sleep on Night 2 at FP1, FP2, F7, and F3, *p*s=.06-.08. Greater injury severity was associated with lower values, i.e., greater sleepiness, for the high alpha/theta ratio with eyes closed post-sleep on Night 1 at T7, P7, and O2, *p*s=.01-.06; high alpha/theta ratio with eyes closed post-sleep on Night 2 at C3, Cz, and Pz, *p*s=.04-.09; total alpha/theta ratio with eyes closed post-sleep on Night 1 at P7, $p=.01$, and O2, $p=.04$; and, total alpha/theta ratio with eyes closed post-sleep on Night 2 at Pz, $p=.09$. Overall, whereas correlations with the alpha/theta ratio for low alpha showed that TBIs with more severe injuries had less sleepiness, correlations with the alpha/theta ratio for high and total alpha showed that TBIs with more severe injuries had greater sleepiness.

Alpha power. Greater injury severity was associated with higher values for **low alpha power** (8-10 Hz) with eyes closed pre-sleep on Night 1 at O1, $p=.05$. On Night 2, greater injury severity was associated with higher values for low alpha power with eyes

closed pre-sleep at FP1, FP2, F7, F8, and T7, *ps*=.04-.08, and post-sleep at FP1, *p*=.09. No group differences or relationships with injury severity were found for **high alpha power** (10-12 Hz) or **total alpha power** (8-12 Hz). A secondary descriptive analysis of the data showed a Group by Medial/Lateral interaction for the fatigue group for high alpha power with eyes closed pre-sleep on Night 1, $F(4,20)=6.53$, $p=.002$, $\eta 2=.57$. Follow-up tests showed group differences at right medial, $F(1,5)=5.47$, $p=.07$, $\eta 2=.52$, and right lateral regions, $F(1,5)=5.39$, $p=.07$, $\eta 2=.52$. Paired t-tests showed that TBIs with daytime fatigue had lower alpha power at P4, $p=.02$, and P8, $p=.02$.

Theta power (4-8 Hz). Greater injury severity was related to greater theta power with eyes closed post-sleep on Night 1 at T7, $r=.42$, $p=.06$, and T8, $r=.39$, $p=.09$. There were no group differences, however, for theta power.

Beta and gamma power. Beta and gamma frequencies were investigated as measures of arousal. Trends toward group main effects suggested that TBIs had more **beta power** (16-25 Hz) overall with eyes open post-sleep on Night 1, $F(1,19)=3.81$, $p=.07$, $\eta 2=.17$, and Night 2, $F(1,18)=3.17$, $p=.09$, $\eta 2=.15$. A secondary analysis of the subgroup means showed effects for the insomnia group pre-sleep on Night 1. Specifically, a trend toward a group main effect showed that TBIs with insomnia had more beta power with eyes closed, $F(1,9)=4.25$, $p=.07$, $\eta 2=.32$. With eyes open, there was a Group by Medial/Lateral interaction for the insomnia group, $F(4,36)=3.22$, $p=.02$, $\eta 2=.26$. This interaction was followed by group differences at left lateral, $F(1,9)=7.43$, $p=.02$, $\eta 2=.45$, right medial, $F(1,9)=9.09$, $p=.02$, $\eta 2=.50$, and right lateral regions, $F(1,9)=7.09$, $p=.03$, $\eta 2=.44$, and trends toward group differences at left medial, $F(1,9)=4.07$, $p=.08$, $\eta 2=.31$, and midline regions, $F(1,9)=3.63$, $p=.09$, $\eta 2=.29$. Paired t-

tests showed that TBIs with insomnia had more beta power at multiple scalp sites (F7, F4, F8, C3, Cz, C4, T8, P7, P3, Pz, P4, P8), *p*s=.003-.09. Given that beta power represents arousal and alertness, it is not surprising that TBIs with insomnia had more beta power.

Gamma power was divided into three frequency bands: low gamma (35-45 Hz), mid-gamma (55-65 Hz), and high gamma (65-75 Hz). With eyes closed post-sleep on Night 1, trends suggested that greater injury severity was associated with less power for **low gamma** at Cz, p=.07, and P7, p=.09, **mid-gamma** at Cz, p=.06, and **high gamma** at Cz, p=.08. With eyes closed pre-sleep on Night 2, however, greater injury severity was associated with greater power for mid-gamma at T7, p=.09, and high gamma at F4, p=.05, and T7, p=.06.

Given the lack of overall group differences, a secondary descriptive analysis of the data was used to understand the impact of sleep complaints. In general, TBIs with insomnia had more gamma power than controls, while TBIs with fatigue had less gamma power, consistent with TBIs' self-reported complaints and previous insomnia literature. Specifically, there was a Group by Anterior/Posterior interaction for the insomnia group for low gamma with eyes closed pre-sleep on Night 1, $F(2,18)=5.86$, p=.01, $\eta 2$=.39, which was followed by group differences at central, $F(1,9)=9.99$, p=.01, $\eta 2$=.53, and parietal regions, $F(1,9)=6.66$, p=.03, $\eta 2$=.43. Paired t-tests showed that TBIs with insomnia had more gamma at most centroparietal sites (C3, C4, T8, P7, P3, P4, P8), *p*s=.01-.06. There was also a Group by Anterior/Posterior interaction for the insomnia group for mid-gamma with eyes closed pre-sleep on Night 1, $F(2,18)=4.09$, p=.03, $\eta 2$=.31, which was followed by group differences central, $F(1,9)=11.25$, p=.01, $\eta 2$=.56,

and parietal regions, $F(1,9)=6.71$, $p=.03$, $\eta 2=.43$. Paired t-tests again showed that TBIs with insomnia had more gamma at most centroparietal sites (T7, C3, Cz, C4, T8, P7, P3, P4, P8), *p*s=.01-.05. A group main effect for high gamma with eyes closed pre-sleep on Night 1 showed that TBIs with insomnia had more gamma overall, $F(1,9)=9.11$, $p=.02$, $\eta 2=.50$.

For low gamma with eyes open pre-sleep on Night 1, there was a Group by Medial/Lateral interaction for the insomnia group, $F(4,36)=4.21$, $p=.01$, $\eta 2=.32$, which was followed by group differences at left lateral, $F(1,9)=9.07$, $p=.02$, $\eta 2=.50$, right medial, $F(1,9)=10.80$, $p=.01$, $\eta 2=.55$, and right lateral regions, $F(1,9)=7.08$, $p=.03$, $\eta 2=.44$, and trends toward group differences at left medial, $F(1,9)=4.68$, $p=.06$, $\eta 2=.34$, and midline regions, $F(1,9)=3.63$, $p=.09$, $\eta 2=.29$. Paired t-tests showed that TBIs with insomnia had more gamma across the scalp (F7, F8, C3, Cz, C4, T8, P7, P3, Pz, P4, P8), *p*s=.002-.07. There was also a Group by Medial/Lateral interaction for the insomnia group for mid-gamma with eyes open pre-sleep on Night 1, $F(4,36)=3.62$, $p=.01$, $\eta 2=.29$, which was followed by group differences at left lateral, $F(1,9)=8.90$, $p=.02$, $\eta 2=.50$, right medial, $F(1,9)=10.33$, $p=.01$, $\eta 2=.53$, and right lateral regions, $F(1,9)=6.06$, $p=.04$, $\eta 2=.40$, and a trend toward a group difference at the left medial region, $F(1,9)=4.40$, $p=.07$, $\eta 2=.33$. Paired t-tests showed that TBIs with insomnia had more gamma across the scalp (F7, F8, T7, C3, C4, T8, P7, P3, P4, P8), *p*s=.002-.08. In addition, there was a Group by Medial/Lateral interaction for the insomnia group for high gamma with eyes open pre-sleep on Night 1, $F(4,36)=2.87$, $p=.04$, $\eta 2=.24$, which was followed by group differences at left lateral, $F(1,9)=10.74$, $p=.01$, $\eta 2=.54$, left medial, $F(1,9)=6.72$, $p=.03$, $\eta 2=.43$, midline, $F(1,9)=5.26$, $p=.05$, $\eta 2=.37$, right medial, $F(1,9)=12.80$, $p=.01$, $\eta 2=.59$,

and right lateral regions, $F(1,9)=8.29$, $p=.02$, $\eta 2=.48$. Paired t-tests showed that TBIs with insomnia had more gamma across the scalp (F7, F4, F8, T7, C3, Cz, C4, T8, P7, P3, Pz, P4, P8), $ps=.003$-$.06$. Finally, there was a Group by Medial/Lateral interaction for the insomnia group for low gamma with eyes open pre-sleep on Night 2, $F(4,36)=3.41$, $p=.02$, $\eta 2=.28$, which was followed by a group difference along the left lateral region, $F(1,9)=5.12$, $p=.05$, $\eta 2=.36$. Paired t-tests showed that TBIs with insomnia had more gamma at F7, $p=.04$, and T7, $p=.09$.

In contrast, trends toward group main effects showed that TBIs with fatigue had less gamma with eyes closed pre-sleep on Night 1 for mid-gamma, $F(1,5)=5.12$, $p=.07$, $\eta 2=.51$, and high gamma, $F(1,5)=5.11$, $p=.07$, $\eta 2=.51$, and with eyes open pre-sleep on Night 1 for mid-gamma, $F(1,5)=4.81$, $p=.08$, $\eta 2=.49$, and high gamma, $F(1,5)=4.91$, $p=.08$, $\eta 2=.50$. Overall, group differences in gamma power were consistent with TBIs' self-reported problems of insomnia or fatigue. See Figures 9 and 10 for means and standard errors for gamma power pre-sleep on Night 1 for TBIs with insomnia and TBIs with fatigue, respectively.

Summary. Group comparisons of waking EEG power were largely non-significant. Ratio measures confirmed self-reported sleep complaints. As expected, TBIs with more severe injuries had greater physiological sleepiness, but this relationship was only true for high and total alpha/theta ratios. The most important finding from these analyses was that TBIs with insomnia had greater beta and gamma power, and that TBIs with fatigue had lower gamma power, supporting evidence of hyperarousal in TBIs with insomnia, and hypoarousal in TBIs with fatigue.

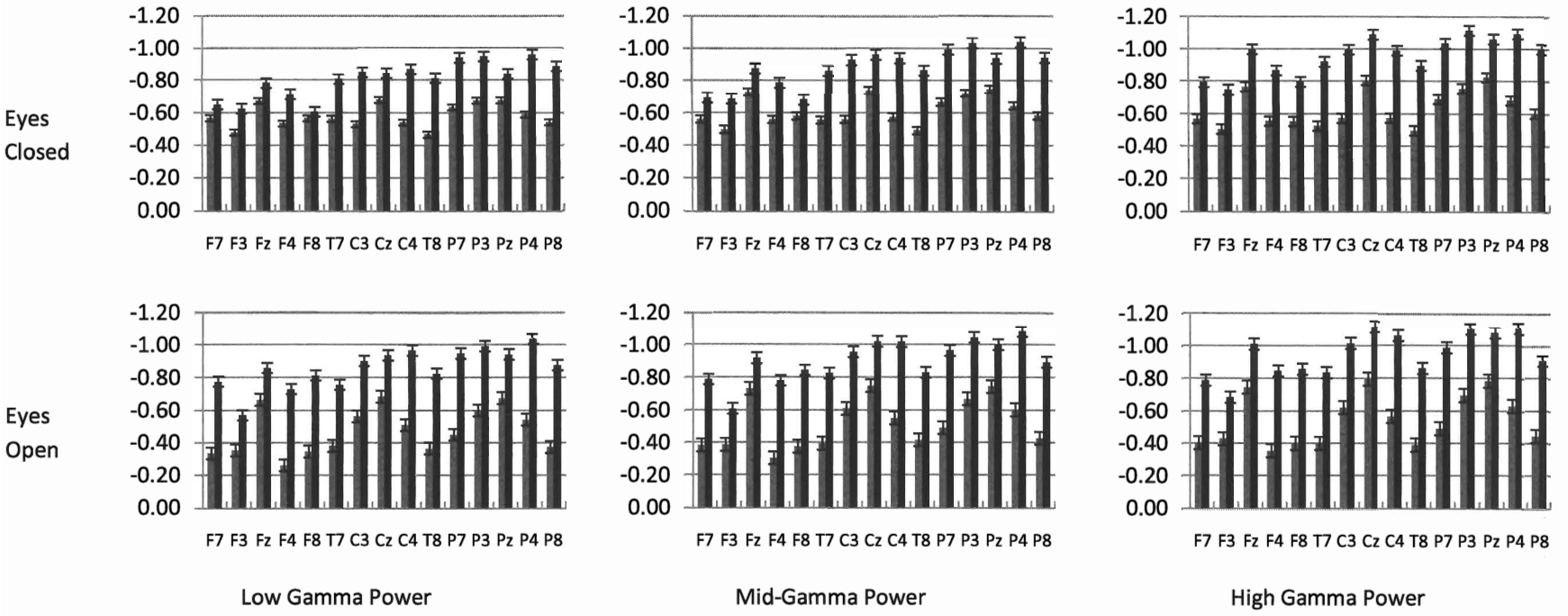


Figure 9. Mean log transformed gamma power ($\mu V/Hz^2$) for TBIs with insomnia (light grey) and controls (black) pre-sleep on Night 1, at each of 15 electrode sites. The top row represents eyes closed sessions; the bottom row represents eyes open sessions. Left panel: low gamma (35-45 Hz) power; centre panel: mid-gamma (55-65 Hz) power; right panel: high gamma (65-75 Hz) power. Standard errors are represented by the error bars on each column. Values closer to zero represent greater power. Note that all comparisons showed that TBIs with insomnia had greater gamma power. The comparison for high gamma power with eyes closed resulted in a significant group main effect; all other comparisons resulted in significant group differences at multiple scalp sites.

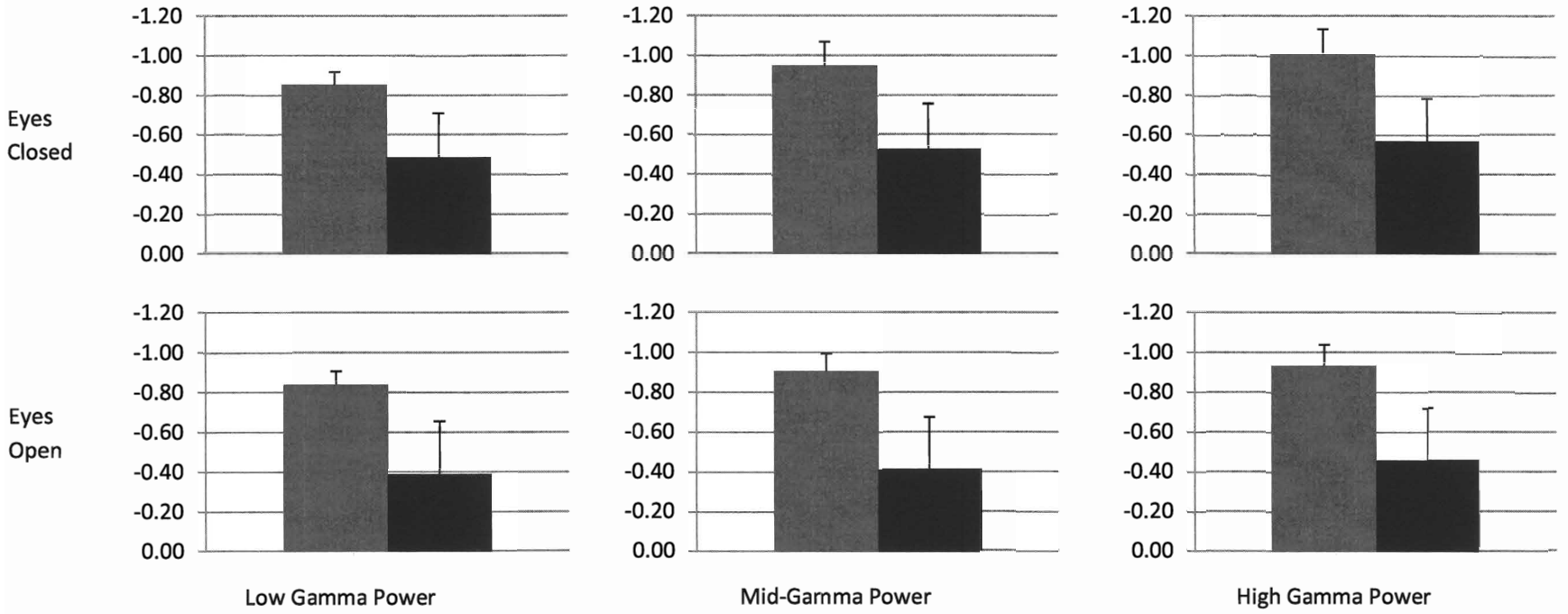


Figure 10. Mean log transformed gamma power ($\mu V/Hz^2$) for TBIs with daytime fatigue (light grey) and controls (black) pre-sleep on Night 1. Group main effects are represented. The top row represents eyes closed sessions; the bottom row represents eyes open sessions. Left panel: low gamma (35-45 Hz) power; centre panel: mid-gamma (55-65 Hz) power; right panel: high gamma (65-75 Hz) power. Standard errors are represented by the error bars on each column. Values closer to zero represent greater power. Note that all comparisons showed that TBIs with daytime fatigue had lower gamma power; comparisons for low gamma did not reach statistical significance.

Waking Event-Related Potentials

Event-related potentials (ERPs) were recorded during the Novel P3, n-back, and visual reaction time tasks at four timepoints across the study. For the Novel P3 task, ERP components were measured to standard, target, and novel stimuli. The N1 and P2 components were measured to standard stimuli; the N1, P2, and classic parietal P300 were measured to target stimuli; and, the N1, P2, and frontal "novel P3" were measured to novel stimuli. For the n-back task, the N1 and P2 components were measured to standard stimuli and the N1, P2, and P300 components were measured to target stimuli. All components were measured at 20 electrode sites. Group (TBI, control) by Anterior/Posterior (frontal, central, parietal) by Medial/Lateral (left lateral, left medial, midline, right medial, right lateral) ANOVAs were run to investigate group differences in ERPs across the scalp. Both group main effects illustrating overall differences between groups and topographic interactions are presented below. Two-tailed tests were used for all comparisons.

For the visual reaction time task, the error-related negativity (ERN) and error positivity (Pe) were elicited in response to errors on this fast-paced task. Individual averages were collapsed across timepoints to form one individual average per participant. The ERN was maximal at FCz, as expected, and thus the ERN and Pe were only measured at this site in the individual averages. Two-tailed paired t-tests were used to compare TBIs (n=15) to controls (n=15) on these components.

Novel P3 task. On Night 2, for **standard stimuli**, a group main effect showed that **N1 latency** was shorter for TBIs compared to controls pre-sleep, $F(1,19)=5.92$, $p=.03$, $\eta 2=.24$, and a trend toward a group main effect showed that N1 latency was

shorter for TBIs compared to controls post-sleep, $F(1,19)=4.10$, $p=.06$, $\eta 2=.18$. Greater injury severity was associated with a shorter N1 latency pre-sleep at F7, T7, and T8, $ps=.05$-$.10$, and post-sleep at T7, $p=.02$. Thus, TBIs had faster encoding of standard stimuli.

Group main effects showed that **P2 latency** was shorter for TBIs compared to controls pre-sleep on Night 1, $F(1,19)=4.66$, $p=.04$, $\eta 2=.20$, and post-sleep on Night 2, $F(1,19)=5.24$, $p=.03$, $\eta 2=.22$; a trend suggested the same post-sleep on Night 1, $F(1,19)=3.22$, $p=.09$, $\eta 2=.15$. There was a Group by Anterior/Posterior interaction for P2 latency pre-sleep on Night 2, $F(2,38)=4.23$, $p=.04$, $\eta 2=.18$. Follow-up ANOVAs showed group differences at frontal, $F(1,19)=9.59$, $p=.01$, $\eta 2=.34$, and parietal regions, $F(1,19)=8.25$, $p=.01$, $\eta 2=.30$. Post hoc tests showed that TBIs had a shorter latency at frontal sites (F7, F3, F4, F8), $ps=.001$-$.03$, and at posterior sites (P3, Pz, P4, P8, O1), $ps=.01$-$.09$. Greater injury severity was associated with a longer P2 latency pre-sleep on Night 1 at T7, $p=.05$, and P8, $p=.04$, pre-sleep on Night 2 at FP1, $p=.03$, and post-sleep on Night 2 at FP2, F4, and F8, $ps=.03$-$.10$. Greater injury severity, however, was associated with a shorter P2 latency pre-sleep on Night 2 at T7, $p=.09$. Most analyses showed that TBIs had a shorter P2 latency, suggesting more efficient inhibition.

There was a significant Group by Anterior/Posterior by Medial/Lateral interaction for **N1 amplitude** pre-sleep on Night 2, $F(8,152)=2.67$, $p=.03$, $\eta 2=.12$. Follow-up tests yielded a Group by Medial/Lateral interaction at the parietal region, $F(4,76)=3.64$, $p=.03$, $\eta 2=.16$. Paired t-tests suggested that TBIs had a larger N1 amplitude at Pz, $p=.04$. Greater injury severity was associated with a larger N1 amplitude pre-sleep on Night 1 at FP2, $p=.06$, but a smaller amplitude post-sleep on Night 1 at P7, $p=.09$, and pre-sleep on

Night 2 at P7, p=.01, and P8, p=.05. Greater injury severity was associated with a larger **P2 amplitude** pre-sleep on Night 1 at P3, P8, and O1, p=.02-.09, post-sleep on Night 1 at O1, p=.03, and O2, p=.06, and pre-sleep on Night 2 at O1, p=.03. Again, TBIs had better encoding and inhibition of standard stimuli.

A secondary descriptive analysis of N1 and P2 to standard stimuli revealed differences for the insomnia and daytime fatigue groups. Specifically, there was a Group by Medial/Lateral interaction for the insomnia group for N1 amplitude post-sleep on Night 1, $F(4,36)=3.51$, p=.02, $\eta 2$=.28, which was followed by a trend toward a group difference at the midline region, $F(1,9)=3.73$, p=.09, $\eta 2$=.29. Paired t-tests showed that TBIs with insomnia had a larger N1 amplitude at Cz, p=.05. A group main effect for the daytime fatigue group for P2 amplitude pre-sleep on Night 1 showed that TBIs had a smaller P2, $F(1,5)=23.01$, p=.01, $\eta 2$=.82.

For target stimuli, greater injury severity was related to a shorter **N1 latency** pre-sleep on Night 1 at frontocentral sites (Fz, F4, F8, T7, C3, T8), ps=.02-.09, post-sleep on Night 1 at F7, p=.05, and T7, p=.001, and post-sleep on Night 1 at FP1, FP2, P7, and O2, ps=.01-.07. Greater injury severity was related to a larger N1 latency post-sleep on Night 1 at O1, p=.07.

A group main effect showed that target **P2 latency** pre-sleep on Night 2 was faster for TBIs than controls, $F(1,19)=5.94$, p=.03, $\eta 2$=.24. Greater injury severity was related to a shorter P2 latency pre-sleep on Night 1 at F3, p=.01, and C3, p=.06, post-sleep on Night 1 at FP2, p=.06, and pre-sleep on Night 2 at FP2, Fz, and P3, ps=.07-.09. Greater injury severity, however, was related to a longer P2 latency post-sleep on Night 1 at Cz, p=.05.

There was a Group by Anterior/Posterior by Medial/Lateral interaction for **P300 latency** post-sleep on Night 1, $F(8,152)=3.41$, $p=.001$, $\eta 2=.15$, and a trend toward a Group by Medial/Lateral interaction pre-sleep on Night 2, $F(4,76)=2.92$, $p=.06$, $\eta 2=.13$. Post-sleep on Night 1, post hoc tests produced a trend toward a group difference at the frontal region, $F(1,19)=4.24$, $p=.05$, $\eta 2=.18$, a Group by Medial/Lateral interaction at the central region, $F(4,76)=3.26$, $p=.03$, $\eta 2=.15$, and a trend toward a Group by Medial/Lateral interaction at the parietal region, $F(4,76)=2.68$, $p=.06$, $\eta 2=.12$. TBIs had a longer P300 latency at a number of sites across the scalp (F7, F4, Cz, C4, T8, P7, P3, P8), *ps*=.002-.10. Pre-sleep on Night 2, post hoc tests produced a trend toward a group difference at right medial sites, $F(1,19)=3.18$, $p=.09$, $\eta 2=.14$. Paired t-tests showed that TBIs had a longer P300 latency at C4, $p=.06$, and P4, $p=.08$. Injury severity was positively correlated with P300 latency pre-sleep on Night 1 at C4, P3, Pz, and O1, *ps*=.01-.06, and pre-sleep on Night 2 at frontocentral sites (FP1, F7, F3, F4, FCZ, T7, C3, O1), *ps*=.02-.09, but negatively correlated with P300 latency post-sleep on Night 2 at F3, $p=.09$. Although shorter latencies for early components suggested faster information processing for TBIs, longer P300 latencies suggested that cognitive processing was slower.

There were interactions between Group and Topography for **N1 amplitude** at most timepoints. Specifically, pre-sleep on Night 1, there was a trend toward a Group by Anterior/Posterior interaction, $F(2,38)=2.83$, $p=.09$, $\eta 2=.13$, and a Group by Medial/Lateral interaction, $F(4,76)=7.28$, $p=.001$, $\eta 2=.28$. Post hoc tests revealed a group difference along the midline, $F(1,19)=6.89$, $p=.02$, $\eta 2=.27$, and a trend toward a group difference at the parietal region, $F(1,19)=3.83$, $p=.07$, $\eta 2=.17$. Paired t-tests showed that

TBIs had a smaller N1 amplitude at several sites (Cz, P3, Pz, P4), *p*s=.01-.08. A trend toward a Group by Anterior/Posterior by Medial/Lateral interaction was found pre-sleep on Night 2, $F(8,152)=2.07$, $p=.09$, $\eta 2=.10$. Post hoc tests revealed a Group by Medial/Lateral interaction at the central region, $F(4,76)=2.83$, $p=.03$, $\eta 2=.13$, and a trend toward the same at the frontal region, $F(4,76)=2.35$, $p=.06$, $\eta 2=.11$. Paired t-tests showed that TBIs had a smaller N1 amplitude at F7, Fz, and Cz, *p*s=.02-.06. Finally, a Group by Medial/Lateral interaction was found post-sleep on Night 2, $F(4,76)=3.26$, $p=.02$, $\eta 2=.15$. Post hoc tests showed a group difference along the midline, $F(1,19)=5.38$, $p=.03$, $\eta 2=.22$. Paired t-tests showed that TBIs had a smaller N1 amplitude at all midline sites (Fz, Cz, Pz), *p*s=.04-.05. Greater injury severity was associated with a larger N1 amplitude pre-sleep on Night 1 at O2, $p=.01$, but a smaller amplitude pre-sleep on Night 2 at P7, $p=.02$. In general, in contrast to standard stimuli, TBIs had smaller N1 amplitudes to target stimuli, compared to controls.

Post-sleep on Night 1, greater injury severity was related to a larger **P2 amplitude** at C4, $p=.07$, but a smaller amplitude at P7, $p=.03$. On Night 2, greater injury severity was related to a larger P2 amplitude pre-sleep at posterior sites (P7, O1, O2), *p*s=.05-.09, and post-sleep at O1, $p=.01$, but a smaller amplitude post-sleep at F8, $p=.06$. Greater injury severity was related to a smaller **P300 amplitude** post-sleep on Night 1 at P7, $p=.06$, and post-sleep on Night 2 at C4, $p=.04$, but a larger amplitude pre-sleep on Night 2 at FP1, $p=.02$.

While few overall group differences emerged for N1 or P2 latency to target stimuli, a secondary analysis of the sleep complaint groups revealed differences for N1 latency. Specifically, post-sleep on Night 1, there was a Group by Anterior/Posterior by

Medial/Lateral interaction for the insomnia group, $F(8,72)=3.89$, $p=.02$, $\eta 2=.30$. Post hoc tests showed a Group by Medial/Lateral interaction at the parietal region, $F(4,36)=11.66$, $p<.001$, $\eta 2=.56$. Paired t-tests showed that TBIs had a shorter latency at P7, $p=.001$. A group main effect post-sleep on Night 2 showed that TBIs with insomnia had a shorter N1 latency than controls, $F(1,9)=7.21$, $p=.03$, $\eta 2=.45$.

When the sleep complaint subgroups were examined, there were also group differences for amplitude measures. Post-sleep on Night 1, there was a Group by Medial/Lateral interaction for the insomnia group for N1 amplitude, $F(4,36)=8.16$, $p<.001$, $\eta 2=.48$. Post hoc tests showed group differences at left medial, $F(1,9)=6.16$, $p=.04$, $\eta 2=.41$, and midline regions, $F(1,9)=5.12$, $p=.05$, $\eta 2=.36$. Paired t-tests showed that TBIs with insomnia had a larger N1 amplitude at C3, $p=.03$, and Cz, $p=.06$.

For P2 amplitude pre-sleep on Night 1, a trend toward a group main effect showed that TBIs with insomnia had a larger P2 amplitude, $F(1,9)=3.69$, $p=.09$, $\eta 2=.29$. There was also a Group by Anterior/Posterior interaction for the daytime fatigue group, $F(2,10)=5.85$, $p=.02$, $\eta 2=.54$. Post hoc tests yielded a group difference at the frontal region, $F(1,5)=6.69$, $p=.05$, $\eta 2=.57$. Paired t-tests showed that TBIs with fatigue had a smaller P2 amplitude at F8, $p=.01$. There was also a Group by Anterior/Posterior interaction for the daytime fatigue group for P2 amplitude pre-sleep on Night 2, $F(2,10)=6.08$, $p=.05$, $\eta 2=.55$. Post hoc tests showed a group difference at the parietal region, $F(1,5)=8.34$, $p=.03$, $\eta 2=.63$. In contrast to Night 1, paired t-tests showed that TBIs with fatigue had a larger P2 amplitude at several sites (P7, P4, P8), $ps=.02$-$.05$. A trend toward a group main effect also suggested that TBIs with insomnia had a larger P300 amplitude than controls pre-sleep on Night 1, $F(1,9)=4.83$, $p=.06$, $\eta 2=.35$.

For **novel stimuli**, there was a Group by Medial/Lateral interaction for **N1 latency** post-sleep on Night 1, $F(4,76)=2.89$, $p=.05$, $\eta 2=.13$. Post hoc ANOVAs showed a group difference at left lateral sites, $F(1,19)=5.96$, $p=.03$, $\eta 2=.24$. Post hoc t-tests showed that TBIs had a shorter latency at P7, $p=.03$. Greater injury severity was related to a longer N1 latency post-sleep on Night 1 at C4, $p=.06$, and P7, $p=.02$, but a shorter latency post-sleep on Night 2 at F4, T8, and Pz, $ps=.01$-$.09$. Greater injury severity was related to a longer **novel P3 latency** pre-sleep on Night 1 at FP2, $p=.05$, and F8, $p=.06$, and post-sleep on Night 1 at P4, $p=.02$, but a shorter latency post-sleep on Night 1 at F7, $p=.04$. In general, there were few consistent relationships between injury severity and latency measures.

A Group by Medial/Lateral interaction was found for **N1 amplitude** pre-sleep on Night 2, $F(4,76)=8.15$, $p<.001$, $\eta 2=.30$. Post hoc tests showed a group difference along the midline, $F(1,19)=8.35$, $p=.01$, $\eta 2=.31$, which was confirmed by paired t-tests showing that TBIs had a smaller amplitude at all midline sites (Fz, Cz, Pz), $ps=.01$-$.07$. On Night 1, greater injury severity was related to a larger N1 amplitude pre-sleep at FP1, $p=.09$, and post-sleep at FP1, $p=.08$, but post-sleep on Night 2, it was related to a smaller amplitude at T8, $p=.06$. Greater injury severity was related to a larger **P2 amplitude** post-sleep on Night 1 at O1, $p=.07$, and pre-sleep on Night 2 at C4, $p=.07$, and P8, $p=.05$.

Greater injury severity was related to a larger **novel P3 amplitude** pre-sleep on Night 1 at O1, $p=.07$, pre-sleep on Night 2 at FP1, FP2, and F7, $ps=.004$-$.09$, and post-sleep on Night 2 at FP1, $p=.06$, and FP2, $p=.07$, but a smaller amplitude post-sleep on Night 1 at F7, $p=.06$, and post-sleep on Night 2 at P7, $p=.07$. Again, few consistent results were found.

A secondary descriptive analysis was used to examine the influence of sleep complaint on the data. For N1 latency pre-sleep on Night 2, there was a trend toward a Group by Anterior/Posterior interaction for the insomnia group, $F(2,18)=3.04$, $p=.07$, $\eta 2=.25$. Post hoc tests yielded a group difference at the parietal region, $F(1,9)=7.09$, $p=.03$, $\eta 2=.44$. Paired t-tests showed that TBIs with insomnia had a shorter N1 latency at P7, $p=.06$, and P8, $p=.01$. For novel P3 latency post-sleep on Night 2, there was a Group by Medial/Lateral interaction for the daytime fatigue group, $F(4,20)=4.76$, $p=.04$, $\eta 2=.49$. Post hoc tests showed a group difference along the left lateral axis, $F(1,5)=7.76$, $p=.04$, $\eta 2=.61$. Paired t-tests showed that TBIs with fatigue had a shorter latency at T7, $p=.03$, and P7, $p=.06$. With respect to amplitude measures, a Group by Anterior/Posterior interaction emerged for the daytime fatigue group for P2 amplitude pre-sleep on Night 2, $F(2,10)=21.02$, $p=.004$, $\eta 2=.81$. Post hoc tests yielded a group difference at the parietal region, $F(1,5)=37.99$, $p=.002$, $\eta 2=.88$. Paired t-tests showed that TBIs with fatigue had a larger P2 amplitude at all parietal sites (P7, P3, Pz, P4, P8), $ps=.01$-$.07$.

In summary, standard stimulus processing was faster and more efficient for TBIs. For novel stimuli, N1 amplitude was smaller for TBIs overall, while P2 amplitude was larger for TBIs with fatigue. Most findings related to target stimuli. N1 and P2 were earlier for TBIs, but P300 latency was longer. TBIs with insomnia had larger N1 and P300 amplitudes, consistent with expectations of hyperattentiveness in this group. TBIs with fatigue showed larger P2 amplitudes, suggesting better inhibition. Results were limited to particular scalp sites.

N-back working memory task. For **standard stimuli,** there was a Group by Anterior/Posterior by Medial/Lateral interaction for **N1 latency** post-sleep on Night 2,

$F(8,152)=2.66$, $p=.04$, $\eta 2=.12$. Post hoc ANOVAs revealed a group difference at the central region, $F(1,19)=5.22$, $p=.03$, $\eta 2=.22$, and a Group by Medial/Lateral interaction at the parietal region, $F(4,76)=2.58$, $p=.07$, $\eta 2=.12$. Paired t-tests indicated that N1 latency was longer for TBIs at Pz, $p=.09$, but shorter for TBIs at several sites (T7, C3, C4, P3), $ps=.01$-$.06$. In addition, on Night 1, greater injury severity was related to a longer N1 latency to standard stimuli pre-sleep at P8, $p=.07$, and a shorter latency post-sleep at T8, $p=.05$.

Greater injury severity was associated with a shorter **P2 latency** to standard stimuli pre-sleep on Night 1 at P3, $p=.02$, pre-sleep on Night 2 at P4, $p=.08$, and post-sleep on Night 2 at FP1, $p=.004$. Greater injury severity was associated with a smaller **P2 amplitude** to standard stimuli post-sleep on Night 2 at O2, $p=.03$.

A secondary descriptive analysis of the sleep complaint subgroups was used to further explore the data. Specifically, for P2 latency to standard stimuli post-sleep on Night 2, a trend toward a group main effect suggested that TBIs with daytime fatigue had a shorter P2 latency than controls, $F(1,5)=4.90$, $p=.08$, $\eta 2=.50$. In addition, TBIs with daytime fatigue had a larger N1 amplitude to standard stimuli than controls post-sleep on Night 1, $F(1,5)=7.20$, $p=.04$, $\eta 2=.59$. In general, results suggested that N1 and P2 were shorter for TBIs, representing efficient information processing.

For **target stimuli**, greater injury severity was associated with a shorter **N1 latency** pre-sleep on Night 1 at P3, $p=.003$, and pre-sleep on Night 2 at FP1, FP2, and F3, $ps=.04$-$.05$; it was associated with a longer latency to target stimuli post-sleep on Night 2 at F4, $p=.08$. Greater injury severity was associated with a shorter **P2 latency** pre-sleep on Night 1 at P3, $p=.02$, but with a longer latency post-sleep on Night 1 at P7, $p=.08$.

Greater injury severity was associated with a longer **P300 latency** post-sleep on Night 1 at F8, p=.05, and pre-sleep on Night 2 at FP1, p=.08; greater injury severity was associated with a shorter P300 latency post-sleep on Night 2 at O1, p=.07. Results showed, in general, that N1 and P2 latency were shorter for TBIs, but that P300 latency was longer. These results are largely consistent with data from the Novel P3 task.

Greater injury severity was associated with a larger **N1 amplitude** post-sleep on Night 1 at O1, p=.09, but a smaller amplitude pre-sleep on Night 2 at Fz, FCz, C3, Cz, and C4, ps=.01-.04. Greater injury severity was associated with a smaller **P2 amplitude** pre-sleep on Night 1 at O1, p=.08, and O2, p=.03, but a larger amplitude post-sleep on Night 1 at FP2, p=.08. Greater injury severity was associated with a smaller **P300 amplitude** pre-sleep on Night 1 at Cz, p=.03, and P7, p=.02, and post-sleep on Night 1 at Cz, p=.04. Again, results showing that N1 amplitude to target stimuli was smaller for TBIs compared to controls was consistent with data from the Novel P3 task.

Given the lack of group differences for ERPs to target stimuli, an exploration of the sleep complaint subgroups provided some further information. A trend toward a group main effect suggested that TBIs with daytime fatigue had a longer N1 latency post-sleep on Night 1, $F(1,5)=6.20$, p=.06, $\eta 2$=.55. As well, a trend toward a group main effect suggested that TBIs with insomnia had a larger P300 amplitude post-sleep on Night 1, $F(1,9)=4.53$, p=.06, $\eta 2$=.34.

In summary, group differences for standard stimuli showed that early encoding was faster for TBIs post-sleep on Night 2. Correlation analyses showed that greater injury severities were associated with faster and more elaborate early encoding. There were no group differences for target stimuli. Correlation analyses showed that greater injury

severities were associated with faster processing; however, evidence of smaller amplitudes suggested less efficient processing of target stimuli.

Visual reaction time task. Only 15 participants in each group were available for statistical comparison; 5 participants in each group committed too few errors to have enough trials for averaging. When the 15 pairs of participants were compared, there were no group differences on measures of **ERN and Pe latency and amplitude.**

Chapter 8: The Relationship between Sleep and Waking Function

The association between sleep variables and measures of waking function was investigated with a number of correlation analyses. Correlations were first run with the TBI group only, to investigate the relationship between sleep disturbance and impairments in waking function. Given that an exhaustive analysis of these relationships would have created a vulnerability to Type I error, analyses were run and interpreted only for relationships that were predicted by theory or a priori hypotheses, or where significant group differences were evident. Parallel analyses were then run for the control group. The purpose of examining correlations in the control group was to determine if correlations were present in the TBI group that did not exist in the control group, and which would therefore reflect the unique relationship between sleep disturbance and waking function, or if correlations existed in the control group were absent in the TBI group, therefore reflecting the absence of typical and/or necessary connections between sleep and waking function. Since the exploration of these relationships required that a number of correlation analyses be run, a more conservative approach was taken, i.e., only effects ($p<.05$) and not trends are reported herein.

The Relationship between Sleep Architecture and Waking Function

Based on group differences in sleep architecture, it was expected that deeper, longer, and more efficient sleep would be related to better waking function in controls, and that poor sleep would be related to poorer waking function in TBIs.

Behavioural variables. For **TBIs**, a number of measures of sleep depth and quality were associated with waking behavioural variables. Relationships showed, in general, that less efficient sleep was associated with worse waking performance. For

instance, a longer sleep onset latency was associated with lower Novel P3 target accuracy on Night 1, r=-.45, p=.05, and with a lower Novel P3 standard accuracy on Night 2, r=-.67, p=.001. Greater amounts of non-rapid eye movement (NREM) sleep were associated with faster reaction times. Specifically, more Stage 4 sleep was associated with a faster n-back reaction time on Night 1, r=-.45, p=.05. More Stage 2 sleep was associated with a faster mean reaction time, r=-.58, p=.01, mean 10% fastest reaction times, r=-.52, p=.02, and mean 10% slowest reaction times, r=-.47, p=.04, on Night 2; thus, more Stage 2 sleep seemed to be related to improved reaction time overall. In contrast, more movement was associated with poorer waking performance, particularly longer reaction times. Specifically, more movement time was related to poorer Novel P3 standard accuracy, r=-.63, p=.003, and to a slower mean reaction time, r=.48, p=.03, greater reaction time standard deviation, r=.60, p=.01, slower mean 10% slowest reaction times, r=.63, p=.003, and greater number of lapses, r=.57, p=.01, all on Night 2. More movement time was related to a slower reaction time to oddball stimuli on Night 3, r=.47, p=.04. Unexpectedly, more wake time was associated with greater oddball accuracy on Night 3. In particular, more wakefulness was related to better standard, r=.54, p=.02, and target oddball accuracy, r=.45, p=.04, on Night 3. More minutes of wake after sleep onset (WASO) was related to better oddball target accuracy on Night 3, r=.45, p=.05. Finally, more REM sleep was associated with a greater number of lapses on the auditory reaction time task on Night 1, r=.48, p=.03. For **controls**, more movement time was associated with poorer n-back standard accuracy on Night 2, r=-.49, p=.03. In general, poorer sleep was associated with poorer waking function in TBIs, but relationships were largely absent for controls.

Subjective variables. For **TBIs**, correlation analyses showed, not surprisingly, that poor sleep was related to poor subjective states in the morning. In particular, a longer sleep onset latency was associated with poorer "best-worst" sleep quality ratings, r=.46, p=.04, and poorer ratings on visual analogue scales (VAS) for happy-sad, r=.47, p=.04, energetic-sluggish, r=.51, p=.02, and relaxed-tense ratings, r=.44, p=.05, on Night 1, and happy-sad, r=.59, p=.01, and relaxed-tense ratings, r=.63, p=.003, on Night 2, showing that taking longer to fall asleep was associated with a poorer mood. More efficient sleep, however, was associated with less sleepiness. For instance, more total sleep time, r=-.46, p=.04, and higher sleep efficiency, r=-.54, p=.02, were associated with less sleepiness at the beginning of the performance assessment battery (PAB) on Night 2; higher sleep efficiency was related to less sleepiness at the end of the PAB on Night 2, r=-.46, p=.04. All relationships listed here suggested that better subjective outcomes followed better quality sleep.

Greater amounts of NREM sleep were, in general, associated with more positive ratings of waking mood. Although more Stage 3 sleep was related to more sleepiness on Night 1, r=.44, p=.05, it was related to less sleepiness, r=-.50, p=.03, and better VAS mood ratings for calm-irritable, r=-.47, p=.04, and energetic-sluggish, r=-.47, p=.04, on Night 2. More Stage 3 sleep was related to better calm-irritable ratings on Night 3, r=-.52, p=.02.

Not surprisingly, indices of wakefulness during the night were associated with greater sleepiness and poorer mood. More WASO was associated with more sleepiness at the beginning of the PAB on Night 2, r=.45, p=.04. More wakefulness, r=.46, p=.04, and more WASO, r=.47, p=.04, were related to more sleepiness at the end of the PAB on

Night 2. More wakefulness was associated with poorer happy-sad ratings on Night 3, r=.53, p=.02. More WASO was related to poorer "best-worst" ratings on Night 3, r=.50, p=.03. More movement time was related to greater fatigue on Night 3, r=.46, p=.04. Finally, more REM sleep was associated with poorer performance ratings, r=.52, p=.03, but less sleepiness at the beginning of the PAB, r=-.49, p=.03, on Night 2. Thus, for TBIs, indices of disrupted sleep were related to poorer waking outcomes.

For **controls**, like TBIs, longer sleep onset latencies were associated with worse moods. A longer sleep onset latency was related to greater fatigue, r=.51, p=.03, poorer VAS mood ratings for calm-irritable, r=.49, p=.03, energetic-sluggish, r=.62, p=.004, and relaxed-tense ratings, r=.48, p=.03, and greater negative affect scores, r=.63, p=.003, all on Night 1. Further, while indices of light sleep were related to various subjective measures for TBIs, for controls these variables were related specifically to poor sleep quality ratings. More wakefulness, r=.55, p=.01, and more WASO, r=.59, p=.01, were related to poorer "best-worst" ratings on Night 3. More WASO was related to poorer composite sleep quality ratings on Night 3, r=.45, p=.05. More Stage 1 sleep was associated with poorer "best-worst" ratings on Night 2, r=.48, p=.03. Finally, whereas greater amounts of NREM were related to better mood for TBIs, for controls, more Stage 2 sleep was related to better "best-worst" ratings on Night 2, r=-.49, p=.03.

Waking electroencephalography (EEG). For **TBIs**, greater amounts of total sleep, NREM, and REM sleep were associated with more physiological sleepiness. Specifically, more total sleep time, r=-.56, p=.01, and higher sleep efficiency, r=-.56, p=.01, were associated with lower values for the low alpha/theta ratio with eyes open on Night 1. More total sleep time, r=-.46, p=.04, and higher sleep efficiency, r=-.46, p=.04,

were also associated with lower values for the total alpha/theta ratio with eyes open on Night 1. These relationships indicate that more efficient sleep was in fact associated with more daytime sleepiness. More REM sleep was also associated with lower values for the low, r=-.59, p=.01, and total alpha/theta ratios with eyes open on Night 1, r=-.51, p=.02, showing that REM sleep was related to greater sleepiness. More Stage 4 sleep was associated with lower values for the low alpha/theta ratio with eyes closed on Night 1, r=-.46, p=.04. More Stage 4 sleep was also associated with lower values for the eyes closed/eyes open ratios for low alpha, r=-.63, p=.004, and total alpha, r=-.51, p=.03, on Night 2. These relationships suggest that Stage 4 was related to greater sleepiness. Wakefulness through the night was associated with less sleepiness. Specifically, more wakefulness, r=.69, p=.001, and more WASO, r=.62, p=.003, were related to higher values for the low alpha/theta ratio with eyes open on Night 1. More wakefulness was associated with higher values for the total alpha/theta ratio with eyes open on Night 1, r=.50, p=.03. Whereas the above relationships were unexpected, more movement was associated with more sleepiness, as hypothesized. More movement time was associated with lower values for the high alpha/theta ratio with eyes closed on Night 1, r=-.47, p=.04, and Night 2, r=-.53, p=.02. More movement time was also associated with lower values for the high alpha eyes closed/eyes open ratio on Night 1, r=-.45 p=.05, and on Night 2, r=-.47, p=.04.

For **controls**, significant results were only found for NREM sleep, and these findings were equivocal. More Stage 3 sleep was related to higher values for the high alpha eyes closed/eyes open ratio on Night 2, r=.51, p=.02, indicating that greater amounts of NREM sleep were associated with less sleepiness. More Stage 4 sleep was

related to lower values for the low, r=-.50, p=.03, and total alpha/theta ratios, r=-.46, p=.04, with eyes open on Night 1. More Stage 4 sleep was related to lower values for the low alpha/theta ratio with eyes closed on Night 2, r=-.47, p=.04, indicating that NREM sleep was associated with more sleepiness.

Waking event-related potentials (ERPs). For the novel P3 task, for **TBIs**, results were inconsistent. While a relationship showing that more Stage 4 sleep was associated with a larger target P300 amplitude on Night 1, r=.60, p=.01, was in line with expectations, i.e., that more efficient sleep would predict better waking performance, more wakefulness was also associated with a larger target P300 amplitude on Night 2, r=.44, p=.05, suggesting the opposite. For **controls**, more Stage 4 sleep was associated with a larger target P300 amplitude on Night 2, r=.54, p=.01, but more REM sleep was associated with a smaller P300 amplitude on Night 1, r=-.49, p=.03, and Night 2, r=-.55, p=.01.

For the n-back task, for **TBIs**, though it was predicted that poor sleep would be related to impaired performance, results were not consistent with hypotheses. Specifically, more total sleep time, r=.61, p=.01, and higher sleep efficiency, r=.61, p=.004, were associated with a longer P300 latency on Night 2, but more wakefulness, r=-.49, p=.03, and more WASO, r=-.64, p=.002, were associated with a shorter P300 latency on Night 1, suggesting relationships opposite to what would be expected. More Stage 2 sleep was associated with a longer P300 latency on Night 1, r=.59, p=.01. One result consistent with expectations was that more Stage 4 sleep was related to a larger P300 amplitude on Night 2, r=.48, p=.03. No relationships were found for **controls** for the n-back task.

For the paired-click paradigm on Night 3, for **TBIs**, more Stage 3 sleep was related to a smaller P50 amplitude to the first stimulus, r=-.47, p=.04. More Stage 3 sleep was also related to a shorter P50 latency to the first, r=-.61, p=.01, and second stimuli, r=-.52, p=.02, suggesting that NREM sleep was related to faster but less extensive processing. For **controls**, a longer sleep onset latency was associated with a larger P50 amplitude to the second stimulus, r=.47, p=.04.

For **controls**, clear results for the oddball task on Night 3 showed that more efficient sleep was related to faster processing in wakefulness, while lighter sleep was associated with slower processing. Specifically, more total sleep time, r=-.51, p=.03, higher sleep efficiency, r=-.53, p=.02, and more Stage 4 sleep, r=-.67, p=.002, were associated with a shorter P300 latency, whereas more Stage 1 sleep was associated with a longer P300 latency, r=.48, p=.04. These relationships were absent for **TBIs**.

Summary. Overall, analyses showed expected relationships for behavioural data for TBIs. Specifically, less efficient sleep was associated with poorer outcomes. This relationship was not found for controls. For both groups, better sleep was associated with improved mood, reduced sleepiness, and better ratings of the previous night's sleep. When quantitative EEG measures of arousal were considered, TBIs showed unexpected patterns in which more sleep and deeper sleep were related to greater sleepiness in the morning. Finally, results for ERP measures showed that deeper and more efficient sleep was related to better oddball task performance for controls, but not for TBIs.

The Relationship between K-Complexes and Waking Function

Based on the notion that K-complexes are sleep-protective, it was expected that greater K-complex densities and larger N550 amplitudes would be related to better

waking function. Given group differences in spontaneous K-complexes, it was expected that these relationships would be found in controls, but absent in TBIs, who had reductions in K-complexes compared to controls.

Behavioural variables. For both groups, higher K-complex densities were associated with faster reaction times. Specifically, a higher K-complex density was related to a faster Novel P3 reaction time on Night 2 for **TBIs**, r=-.61, p=.01, and **controls**, r=-.52, p=.02.

Subjective variables. For **TBIs**, greater densities were related to poorer outcomes. A higher K-complex density was related to poorer subjective ratings of sleep onset latency, r=.72, p<.001, and total sleep time, r=-.58, p=.01, on Night 1. For **controls**, a higher K-complex density was related to poorer "best-worst", r=.49, p=.03, and relaxed-tense ratings, r=.51, p=.02, on Night 2. A higher K-complex density was also associated with poorer composite sleep quality scores on Night 2, r=.50, p=.03. A larger N550 amplitude was associated with a lower number of estimated awakenings on Night 3, r=-.50, p=.03. Thus, greater K-complex densities were associated with worse subjective ratings for both groups.

Waking EEG. No relationships were found for either group.

Waking ERPs. For the Novel P3 task, for **TBIs**, a higher K-complex density was associated with a larger target P300 amplitude on Night 2, r=.57, p=.01, suggesting that K-complexes were predictive of more efficient waking information processing and attention. No relationships were found for **controls** for the Novel P3 task. No relationships were found for the n-back task for either group. For controls only, a larger

N550 amplitude was associated with a longer waking oddball target P300 latency on Night 3, r=.57, p=.01.

Summary. Overall, there were few relationships between K-complexes and waking function. Results suggested that more K-complexes were related to faster and more extensive waking processing, but poorer subjective ratings, for both groups. Thus, there was some evidence to support hypotheses for the relationship between K-complexes and waking function.

The Relationship between Sleep Spindles and Waking Function

Based on the notion that sleep spindles are inhibitory, it was predicted that greater spindle densities and longer spindle durations would be associated with intact waking function. Given the hypothesis that TBIs experience a breakdown in inhibition, it was expected that positive relationships between spindles and waking function would be found in controls, but absent in TBIs.

Behavioural variables. For both groups, relationships between sleep spindles (both density and duration) and waking function were equivocal, where some variables suggested better waking function and others suggested poorer waking function. For **TBIs**, several relationships showed spindles to be related to intact waking function. A higher Stage 3 spindle density was associated with a greater Novel P3 target accuracy on Night 1, r=.45, p=.05. A higher Stage 2 spindle density was associated with a greater Novel P3 target accuracy on Night 2, r=.54, p=.01. A longer Stage 2 spindle duration, r=-.55, p=.01, and Stage 3 spindle duration, r=-.47, p=.04, were associated with a shorter n-back reaction time on Night 2. In contrast, other relationships showed spindles to be related to poor waking function. A higher Stage 3 spindle density was associated with poorer

accuracy to oddball standard stimuli on Night 3, r=-.49, p=.03. A longer Stage 4 spindle duration was associated with poorer Novel P3 standard accuracy on Night 2, r=-.45, p=.05.

For **controls**, a longer Stage 2 spindle duration, r=-.49, p=.03, and Stage 3 spindle duration, r=-.51, p=.02, were related to a shorter n-back reaction time on Night 1, suggesting that spindles were related to intact waking performance. On the contrary, a longer Stage 2 spindle duration was related to a poorer Novel P3 novel accuracy on Night 1, r=-.50, p=.03.

Subjective variables. In contrast to the equivocal nature of relationships with behavioural performance, relationships with subjective ratings clearly showed, for both groups, that sleep spindles were associated with poorer mood and poorer sleep quality ratings. These relationships were in contrast to what was predicted about the relationship between sleep spindles, as markers of efficient sleep, and waking function. Specifically, for **TBIs**, density measures showed that spindles were predictive of poorer outcomes. A higher Stage 4 spindle density was associated with poorer relaxed-tense ratings on Night 2, r=.45, p=.05. A higher Stage 3 spindle density was associated with poorer energetic-sluggish ratings on Night 3, r=.47, p=.04.

Indices of spindle duration showed the same effects. A longer Stage 4 spindle duration was associated with estimates of longer sleep onset latencies on Night 1, r=.52, p=.02, Night 2, r=.62, p=.01, and Night 3, r=-.59, p=.01; with poorer "best-worst" ratings on Night 1, r=.54, p=.01; and with estimates of less total sleep time on Night 2, r=-.47, p=.04. A longer Stage 4 spindle duration was also associated with greater fatigue, r=.57, p=.01, and greater sleepiness, r=.47, p=.04, on Night 3. A longer Stage 2 spindle

duration, r=.49, p=.03, and Stage 3 spindle duration, r=.46, p=.04, were related to poorer happy-sad ratings on Night 2. A longer Stage 2 spindle duration, r=.54, p=.01, and Stage 3 spindle duration, r=.54, p=.01, were also related to poorer relaxed-tense ratings on Night 2. Last, a longer Stage 2 spindle duration was related to poorer calm-irritable ratings on Night 1, r=.53, p=.02. In sum, for TBIs, greater spindle density and longer spindle duration were related to poorer subjective outcomes, in contrast with expectations.

For **controls**, as well, spindle density was associated with poorer subjective ratings. A higher Stage 3 spindle density, r=-.51, p=.02, and Stage 4 spindle density, r=-.50, p=.03, were related to lower positive affect scores on Night 1. A higher Stage 4 spindle density was related to greater sleepiness at the beginning, r=.45, p=.05, and end of the PAB, r=.52, p=.02, greater fatigue, r=.51, p=.02, poorer energetic-sluggish ratings, r=.51, p=.02, and higher negative affect scores, r=.53, p=.02, all on Night 2. A higher Stage 4 spindle density was also related to poorer energetic-sluggish ratings on Night 3, r=.49, p=.04. A higher Stage 3 spindle density was related to poorer calm-irritable ratings on Night 1, r=.48, p=.03. A higher Stage 3 spindle density was also related to greater sleepiness at the end of the PAB, r=.48, p=.03, greater fatigue, r=.52, p=.02, poorer VAS mood ratings for calm-irritable, r=.64, p=.002, happy-sad, r=.60, p=.01, and energetic-sluggish, r=.61, p=.01, higher negative affect score, r=.66, p=.002, and poorer composite sleep quality scores, r=.50, p=.03, all on Night 2. A higher Stage 2 spindle density was associated with poorer performance ratings on Night 1, r=-.61, p=.01. A higher Stage 2 spindle density was also related to greater sleepiness at the end of the PAB on Night 1, r=.47, p=.04. A higher Stage 2 spindle density was related to greater sleepiness, r=.45,

p=.05, poorer happy-sad ratings, r=.53, p=.02, higher negative affect scores, r=.48, p=.03, and poorer composite sleep quality scores, r=.56, p=.01, on Night 2. These relationships illustrated that, for controls, greater spindle densities were associated with poorer subjective outcomes.

With respect to spindle duration, a longer Stage 4 spindle duration, r=.46, p=.05, and Stage 2 spindle duration, r=.61, p=.01, were associated with poorer composite sleep quality scores on Night 1. A longer Stage 4 spindle duration was associated with poorer calm-irritable ratings on Night 3, r=-.55, p=.02. A longer Stage 2 spindle duration was associated with greater fatigue, r=.45, p=.05, and poorer energetic-sluggish ratings, r=.50, p=.02, on Night 3. Thus, similar to TBIs, longer spindle durations were related to poorer outcomes for controls.

Waking EEG. Consistent with behavioural and subjective data, sleep spindles were related to greater EEG sleepiness for both groups. This result was inconsistent with the hypothesis that reductions in sleep spindles in TBIs would be related to poorer waking function. For **TBIs**, density and duration measures showed this relationship. A higher Stage 2 spindle density was associated with lower values for the eyes closed/eyes open ratio for high alpha on Night 2, r=-.56, p=.01. A longer Stage 4 spindle duration was associated with lower values for the eyes closed/eyes open ratio for total alpha on Night 2, r=-.47, p=.04. A longer Stage 3 spindle duration was associated with lower values for the eyes closed/eyes open ratio for total alpha on Night 2, r=-.50, p=.03. A longer Stage 2 spindle duration was associated with lower values for the eyes closed/eyes open ratio for total alpha on Night 2, r=-.50, p=.03.

For **controls**, a longer Stage 3 spindle duration was associated with lower values for the eyes closed/eyes open ratio for total alpha, r=-.45, p=.05, and with the total alpha/theta ratio with eyes closed, r=-.47, p=.04, on Night 2. Thus, for both groups, sleep spindles were associated with greater EEG sleepiness.

Waking ERPs. Despite all other relationships with sleep spindles showing unexpectedly that spindles were associated with poorer waking function, relationships with waking ERPs showed that sleep spindles were related to positive outcomes. For **TBIs**, these relationships were true for most ERP tasks. For the Novel P3 task, a higher Stage 2 spindle density was associated with a shorter novel P3 latency on Night 1, r=-.66 p=.002. A longer Stage 2 spindle duration was associated with a shorter target P300 latency on Night 2, r=-.47, p=.04. For the paired-click paradigm on Night 3, a higher Stage 3 spindle density was associated with a larger P50 amplitude to the first stimulus, r=.49, p=.03. A longer Stage 4 spindle duration was associated with a larger P50 amplitude to the first stimulus, r=.50, p=.03. For the n-back task, however, a higher Stage 4 spindle density was related to a longer P300 latency on Night 1, r=.460, p=.04. For **controls**, a longer Stage 3 spindle duration was related to a larger n-back P300 amplitude on Night 1, r=.49, p=.03. For the paired-click paradigm on Night 3, a higher Stage 4 spindle density was related to a larger waking P50 amplitude to the first, r=.46, p=.05, and second stimuli, r=.42, p=.03.

Summary. Some variables were related to good waking function, while others were related to poor function. In contrast to expectations, sleep spindles were associated with poor subjective ratings and greater EEG sleepiness, in both groups. While analyses

also showed that sleep spindles were associated with intact waking ERPs, these relationships were only expected to be found in controls, but were present in both groups.

The Relationship between Delta Power and Waking Function

Based on the knowledge that delta power reflects sleep homeostasis, greater delta power, i.e., deeper sleep, was expected to be associated with intact waking function. Given predictions of impairments in sleep homeostatic processes in TBIs and robust group differences in this variable, the relationship between delta power and waking function was expected to be absent for TBIs.

Behavioural variables. No relationships were found for either group.

Subjective variables. For both groups, greater delta power was associated with worse subjective outcomes. For **TBIs,** greater delta power was associated with poorer energetic-sluggish ratings on Night 1, r=.47, p=.04. For **controls**, greater delta power was associated with poorer relaxed-tense ratings, r=.47, p=.04, and higher negative affect scores, r=.52, p=.02, on Night 1. Greater delta power was also related to longer subjective estimates of sleep onset latency on Night 2, r=.45, p=.05.

Waking EEG. For both groups, greater delta power was associated with greater EEG sleepiness. For **TBIs**, greater delta power was associated with lower values for the eyes closed/eyes open ratio for low alpha on Night 2, r=-.46, p=.05. For **controls**, greater delta power was associated with lower values for the alpha/theta ratio with eyes closed for low alpha, r=-.45, p=.05, and with eyes open for low, r=-.49, p=.03, high, r=-.44, p=.05, and total alpha, r=-.51, p=.02, all on Night 1.

Waking ERPs. Contrary to other waking function measures, greater delta power was related to better waking ERP performance on the Novel P3 task for both groups.

Specifically, for **TBIs**, greater delta power was associated with a larger target P300 amplitude on Night 1, r=.45, p=.05, and Night 2, r=.58, p=.01. Greater delta power was associated with a shorter target P300 latency on Night 2, r=-.48, p=.03. For **controls,** greater delta power was associated with a larger target P300 amplitude on Night 1, r=.57, p=.01, and Night 2, r=.48, p=.03. For the n-back task, no relationships were found for TBIs or controls.

Summary. In general, few relationships were found to link delta power to waking function. Contrary to expectations, more delta power was related to poorer subjective outcomes and greater EEG sleepiness for both groups. Greater delta power, however, was related to better waking ERP performance on one task. Although this relationship was consistent with expectations, it was predicted to exist only for controls, but was found for both groups.

The Relationship between Gamma Power and Waking Function

Given previous research showing that gamma power represents hyperarousal, it was expected that greater gamma power in sleep, representing disrupted sleep, would be related to poorer waking function. Based on the expectation that increases in gamma power would characterize the sleep of TBIs but not controls, it was predicted that the relationship between gamma power in sleep and waking function would only be found for TBIs.

Behavioural variables. Consistent with expectations, no relationships were found for **controls.** In contrast to expectations, however, greater gamma power was associated with better behavioural performance for **TBIs**. In particular, greater high gamma power was related to better Novel P3 novel accuracy on Night 1, r=.47, p=.04. Greater high

gamma power was related to a smaller reaction time standard deviation on Night 1, r=-.45, p=.05.

Subjective variables. In general, greater gamma power was associated with poorer subjective ratings. Although predicted for TBIs specifically, this relationship was found for both groups. For **TBIs**, greater low gamma power was related to poorer energetic-sluggish ratings on Night 1, r=.47, p=.04, and Night 2, r=.62, p=.004. For **controls**, greater high gamma power was related to greater fatigue, r=.49, p=.03, and poorer "best-worst" ratings, r=.52, p=.02, but a lower estimated number of awakenings, r=-.47, p=.04, all on Night 2.

Waking EEG. No relationships were found for **TBIs.** For **controls,** correlation analyses revealed that greater gamma power was associated with greater physiological sleepiness. Greater low gamma power was associated with lower values for the eyes closed/eyes open ratio for low, r=-.52, p=.02, and total alpha, r=-.46, p=.04, on Night 2. Greater low, r=-.53, p=.02, and high gamma, r=-.50, p=.02, were associated with lower values for the alpha/theta ratio with eyes closed for low alpha on Night 2. Greater low gamma power was also associated with lower values for the alpha/theta ratio with eyes closed for total alpha on Night 2, r=-.46, p=.04. These relationships were consistent with the expectation that greater gamma power would be associated with greater sleepiness. It was surprising, however, that this relationship was found for controls and not TBIs.

Waking ERPs. For the Novel P3 task, for **TBIs**, gamma power was predictive of better functioning. Specifically, greater low, r=.56, p=.01, and high gamma power, r=.46, p=.04, were associated with a larger target P300 amplitude on Night 1. Greater high gamma power was related to a shorter novel P3 latency on Night 2, r=-.59, p=.01. Thus,

surprisingly, greater gamma power for TBIs was associated with better waking performance. For **controls,** no relationships were found for the Novel P3 task. For the n-back task, no relationships were found for TBIs or controls.

Summary. Overall, results for gamma power were inconsistent with expectations. Specifically, greater gamma power was associated with better behavioural and ERP performance for TBIs, inconsistent with the notion that hyperarousal would be related to poor waking function. While greater gamma power was related to poorer subjective outcomes, as expected, this relationship existed for both groups although only predicted for TBIs. Greater gamma power was also associated with greater sleepiness in controls, but not TBIs.

The Relationship between Paired-Click Paradigm ERPs and Waking Function

Based on previous research showing that TBIs had deficits in sensory gating and other research showing the connection between sensory gating in wakefulness and sleep, it was expected that poor sensory gating in sleep on Night 3 would be related to poor waking function for TBIs in the morning following the third night. Intact sensory gating was expected to be related to intact waking function for controls.

Behavioural variables. For **TBIs**, a larger REM P50 suppression value, i.e., poor gating, was related to poorer waking oddball target accuracy, r=-.51, p=.02. No relationships were found for **controls.**

Subjective variables. For **TBIs**, results generally confirmed hypotheses. A larger P50 amplitude to the first stimulus in REM was associated with greater fatigue, r=.57, p=.01, poorer calm-irritable ratings, r=.46, p=.05, poorer composite sleep quality ratings, r=.46, p=.05, and lower total sleep time estimates, r=-.62, p=.01. A larger P50 amplitude

to the first, r=.74, p=.001, and second stimuli, r=.60, p=.01, in REM were both related to longer sleep onset latency estimates. In Stage 2, a larger P50 amplitude to the first stimulus was associated with poorer happy-sad ratings, r=.48, p=.04, and a larger P50 suppression ratio was associated with poorer relaxed-tense ratings, r=.52, p=.02. A larger P50 amplitude to the second stimulus was related to longer sleep onset latency estimates, r=.50, p=.04. Overall, for TBIs, results were consistent with expectations that difficulties with inhibition in sleep would be related to poor waking function. For **controls**, in REM, a longer P50 latency to the second stimulus was related to greater fatigue, r=.47, p=.04.

Waking P50. For **TBIs**, results again suggested that waking function was related to information processing in sleep. In REM, a larger P50 amplitude to the second stimulus was associated with a larger waking P50 amplitude to the first stimulus, r=.47, p=.05, and with a longer waking P50 latency to the second stimulus, r=.54, p=.02. In Stage 2, a larger P50 amplitude to the second stimulus was related to a longer waking P50 latency to the second stimulus, r=.46, p=.05. In general, over-processing of stimuli during sleep was related to slower and more elaborate processing in wakefulness. For **controls**, in REM, a longer P50 latency to the first stimulus was related to a smaller waking P50 amplitude to the first stimulus, r=-.45, p=.05. In Stage 2, a larger P50 amplitude to the first stimulus was related to a larger waking P50 amplitude to the second stimulus, r=.60, p=.01. Thus, greater stimulus processing in sleep was associated with greater processing in wakefulness. While more elaborate stimulus processing is considered desirable for other ERP tasks, for the paired-click paradigm elaborate processing, especially of the second stimulus, is considered a marker of sensory gating impairments and thus considered an index of inefficient stimulus encoding.

Summary. Though there was a paucity of significant correlations for behavioural data, one result suggested that poor gating in sleep was related to low accuracy in wakefulness for TBIs. Several relationships showed that over-processing of stimuli in sleep was related to poor subjective outcomes for TBIs. More extensive stimulus processing in sleep was also related to more extensive, but slower, stimulus processing in wakefulness for TBIs. For controls, more extensive stimulus processing in sleep was related to more extensive processing in wakefulness. Overall, results for the paired-click paradigm largely supported hypotheses.

The Relationship between Oddball Paradigm ERPs and Waking Function

The oddball task on Night 3 was employed to measure information processing in sleep. For controls, intact information processing in sleep, e.g., small N1, large P2, large N350, was expected to relate to intact waking function. For TBIs, impairments in information processing in sleep were expected to relate to deficits in waking function.

Behavioural variables. Correlation analyses yielded few relationships between oddball ERPs and behavioural performance. For **TBIs**, in REM, a longer N350 latency was associated with a shorter waking reaction time, r=-.52, p=.02. In Stage 2, a longer N1 latency was associated with poorer waking target accuracy, r=-.57, p=.01. For **controls**, in REM sleep, a larger N1 amplitude was associated with poorer waking standard accuracy, r=.73, p=.001. The relationship for controls was consistent with expectations, though the results for TBIs were not.

Subjective variables. For **TBIs**, in general, longer latencies and larger N350 amplitudes were associated with better subjective outcomes. Specifically, in REM, a longer P2 latency was associated with better energetic-sluggish ratings, r=-.46, p=.05. In

Stage 2, a longer P2 latency, r=-.70, p=.001, and a longer N350 latency, r=-.47, p=.04, were associated with better happy-sad ratings. A longer N350 latency was associated with less fatigue, r=-.65, p=.003, and better energetic-sluggish ratings, r=-.52, p=.02. A larger N350 amplitude was associated with better "best-worst" ratings, r=.49, p=.03, and better composite sleep quality ratings, r=.47, p=.05. In general, longer latencies were associated with better mood and reduced fatigue, while larger N350 amplitudes, representing more efficient sleep, were associated with better sleep quality ratings.

For **controls**, results were largely consistent with results for TBIs. In REM, a longer N1 latency was associated with better energetic-sluggish ratings, r=-.52, p=.02. A longer P2 latency was associated with less fatigue, r=-.53, p=.02, and better energetic-sluggish ratings, r=-.54, p=.02. A larger P2 amplitude was associated with better calm-irritable ratings, r=-.47, p=.04, and longer estimates of total sleep time, r=-.55, p=.02. In Stage 2, a longer P2 latency was associated with poorer "best-worst" sleep quality ratings, r=.46, p=.05. A larger P2 amplitude was associated with a greater estimated number of awakenings, r=.56, p=.01. Consistent with results for TBIs, longer latencies, representing slower information processing, were associated with better subjective outcomes. Larger P2 amplitudes, representing greater inhibitory processes, were associated with higher estimates of number of awakenings.

Waking ERPs. For **TBIs**, results showed relationships between information processing in sleep and wakefulness. In REM, a longer N1 latency was related to a longer waking P2 latency, r=.49, p=.03, and waking P300 latency, r=.47, p=.05. In Stage 2, a longer N1 latency was related to a longer waking P2 latency, r=.47, p=.04. A larger P450 amplitude was related to a shorter waking P300 latency, r=-.46, p=.05, and larger waking

N1 amplitude, r=-.49, p=.04. Thus, for TBIs, longer latencies in sleep were associated with longer latencies in wakefulness. A larger P450, a sleep-specific component, was associated with faster and more extensive processing in wakefulness.

For **controls**, results also showed relationships between sleep and waking ERPs. In REM, a longer N1 latency was related to a longer waking P2 latency, r=.49, p=.04. Again in REM, a longer P2 latency, r=.48, p=.04, was related to a longer waking P300 latency. A larger N350 amplitude was associated with a shorter waking P300 latency, r=.52, p=.02. In Stage 2, a longer P2 latency was associated with a smaller waking P2 amplitude, r=-.48, p=.04. A larger N350 amplitude was associated with a longer waking N1 latency, r=-.49, p=.03, and P2 latency, r=-.46, p=.05. Like TBIs, longer latencies in sleep were associated with longer latencies and less extensive processing in wakefulness. Results for N350 amplitude were equivocal.

Summary. Few relationships were found for behavioural data. For both groups, however, longer latencies were associated with better subjective outcomes. For TBIs, larger N350 amplitudes, i.e., efficient sleep, were also associated with better outcomes, but for controls, larger P2 amplitudes, representing inhibition, were associated with lower sleep quality ratings. With respect to ERP data, longer latencies of components in sleep were associated with longer latencies of components in wakefulness, for both groups. Larger P450 amplitudes were associated with faster and more extensive processing in wakefulness for TBIs. Results for N350 amplitude were equivocal for controls.

Chapter 9: Discussion

Individuals with a history of traumatic brain injury (TBI) often complain of problems sleeping and daytime fatigue (e.g., Ouellet et al., 2004). Recent work (e.g., Ouellet et al., 2006) has confirmed through survey data that the incidence of insomnia is higher in a group of individuals with a TBI than in the general population. Orff et al. (2009) provided a comprehensive review of the literature, which outlined numerous factors that may contribute to the development of sleep disruption in this population. Research has been limited, however, in identifying the neurophysiological underpinnings of sleep disruption in TBI. A number of older studies (e.g., Grossman, 1949; Lenard & Pennigstorff, 1970) identified specific changes to the sleep of individuals with a history of head injury, including decreases in K-complexes and extension of sleep spindles. Electroencephalography (EEG) techniques, however, have rarely been employed to study the neurophysiological changes to the sleep of individuals with a TBI. Thus, in this study, a variety of measures (sleep architecture, sleep phasic events, quantitative EEG, and event-related potentials) were examined in order to better understand the changes to sleep physiology that occur in TBI.

In general, the goals of this investigation were to determine if the sleep complaints associated with TBI are due to impairments in inhibition and gating. Specifically, the goals were to investigate changes to sensory gating and information processing, and to understand alterations in sleep/wake homeostatic regulation that occur with TBI. These changes were expected to reflect the presence of hyperarousal, a breakdown in inhibition and gating, and dysregulation in homeostatic sleep pressure. Individuals with a TBI were compared to age-matched controls on three protocol nights.

The first and second nights served as recording nights; participants' sleep was recorded throughout the night. The third night was a stimulus delivery night; pitch oddball and paired-click paradigms were used to record event-related potentials (ERPs) in all stages of sleep.

Previous reports (e.g., George & Landau-Ferey, 1986; Grossman, 1949; Harada et al., 1976; Kaufman et al., 2001; Lenard & Pennigstorff, 1970; Makley et al., 2008, 2009; Schreiber et al., 2008) have shown that individuals with a TBI have poorer sleep. Thus, it was expected that those with a TBI in this study would also have poorer sleep than controls on sleep architecture measures. Previous research (Amzica & Steriade, 2000; Halasz, 1981; Halasz et al., 1985; Steriade, 2000) has provided experimental evidence that K-complexes are inhibitory, and neurobiological (Amzica & Steriade, 2000; Steriade, 2000) and ERP (Cote et al., 2000; Elton et al., 1997) studies have also shown that sleep spindles are inhibitory. Studies investigating K-complexes in TBI have been scarce (see Grossman, 1949), and those measuring sleep spindles have been equivocal (e.g., Harada et al., 1976; Lenard & Pennigstorff, 1970). However, based on the knowledge that K-complexes and sleep spindles are inhibitory, it was predicted that both phasic events would be reduced in number and smaller, i.e., smaller N550 amplitude, shorter spindle duration, in those with a TBI compared to controls.

Some evidence has shown that there are differences in quantitative EEG (qEEG) in head injury that suggest impairments in homeostatic processes (e.g., Parsons et al., 1997). Based on Borbely's (1982) work showing the relationship between delta EEG power and homeostatic sleep pressure, it was predicted that individuals with a TBI in this study would have lower delta power in sleep, suggesting a homeostatic dysregulation.

Previous literature on insomnia has illustrated that beta and gamma EEG power, as markers of hyperarousal, are elevated in individuals with insomnia (e.g., Bonnet & Arand, 1997; Perlis et al., 2005). Given the prevalence of insomnia in TBI, it was hypothesized that individuals with a TBI would have greater beta and gamma power, indicating that they were hyperaroused. These elevations were hypothesized to occur in both sleep and wakefulness, mirroring the 24-hour hyperarousal that has been found with insomniacs.

Event-related potential paradigms delivered throughout the night were expected to show impairments in information processing for individuals with a TBI. Specifically, given previous research documenting sensory gating impairments in wakefulness in those with a TBI (Arciniegas et al., 1999, 2000, 2001; Arciniegas & Topkoff, 2004), it was predicted that individuals with a TBI in this study would show evidence of poor gating. Previous researchers (e.g., Kisley et al., 2003) have suggested that poor gating in wakefulness extends into sleep. Thus, it was hypothesized that individuals with a TBI would show poor gating in wakefulness and sleep.

Second, based on previous research investigating neurocognitive processing in those with a TBI with ERPs (e.g., Lew et al., 2004; Rugg et al., 1993; Segalowitz et al., 2001; Solbakk et al., 1999, 2002), it was hypothesized that those with a TBI would show impairments in information processing. Previous research in ERPs in sleep has shown that individuals with insomnia were hyperattentive to stimuli (e.g., Bastien et al., 2008; Devoto et al., 2003, 2005; Kertesz & Cote, in press; Yang & Lo, 2007). Based on the prevalence of insomnia in TBI, it was predicted that individuals with a TBI in this study would show hyperattentiveness.

Finally, there is a great deal of previous literature documenting deficits in waking function in TBI (e.g., Asloun et al., 2008; Mathias, Beall et al., 2004; Rugg et al., 1993; Segalowitz et al., 2001). Measures used in previous literature include classic neuropsychological tests, as well as laboratory-based cognitive testing. It was expected that results would confirm deficits in those with a TBI on both types of measures, consistent with previous literature. It was also hypothesized that indices of sleep disruption would be related to waking deficits in those with a TBI, and that the relationship between sleep and waking function would be different for controls.

Sleep Dysregulation and Disruption in TBI

Consistent with hypotheses, those with a TBI showed evidence of poorer sleep. Sleep was lighter and less efficient, confirming previous research (e.g., George & Landau-Ferey, 1986; Grossman, 1949; Harada et al., 1976; Kaufman et al., 2001; Lenard & Pennigstorff, 1970; Makley et al., 2008, 2009; Schreiber et al., 2008). Specifically, individuals with a TBI took longer to fall asleep, and had less Stage 2 sleep, less total sleep time, lower sleep efficiency, and more movement. Subgroup analyses showed that individuals with a TBI with insomnia had more Stage 1 sleep. Greater injury severity was associated with more Stage 1 sleep, and lower sleep efficiency. Group differences in the amount of night-to-night variability were consistent with predictions that the sleep of those with a TBI would be less stable. In general, evidence existed on all three nights showing that those with a TBI had poorer sleep than controls. Although a number of studies have used polysomnography to investigate sleep in TBI (e.g., George & Landau-Ferey, 1986; Grossman, 1949; Harada et al., 1976; Kaufman et al., 2001; Lenard & Pennigstorff, 1970; Manseau, 1996; Schreiber et al., 2008; Williams et al., 2008), the

current study is the only to date to provide such a comprehensive investigation across three consecutive nights in the laboratory, in a group of individuals with a variety of sleep complaints across a range of injury severities.

Spontaneous K-complex density was calculated for Stage 2 on Nights 1 and 2. There was strong evidence that those with a TBI had fewer spontaneous K-complexes than control participants on both Night 1 and Night 2. As well, the average interval between K-complexes was calculated. The standard deviation of this interval was calculated as a measure of variability. On Night 1, individuals with a TBI had a larger average interval, indicating that K-complexes occurred further apart in time, consistent with the finding of fewer K-complexes. There was also a larger standard deviation for this interval, suggesting disruption to the rhythmicity of K-complex generation in TBI. These findings suggest a breakdown in the generation of K-complexes in TBI, and may represent a disruption in sleep-protective mechanisms. In addition to the group difference in K-complex density, there was also evidence to suggest a breakdown in the rhythmicity of K-complex generation. The strength of these results suggests that disruption to sleep-protective mechanisms may be the most salient problem affecting sleep in those with a TBI. Bastien et al.'s (2009) recent paper stating no differences in K-complexes between psychophysiological insomniacs and controls allows us to clearly state that, while individuals with a TBI may complain of insomnia-like symptoms, the sleep physiology is distinct from that of insomniacs.

K-complexes were also evoked to target stimuli in Stage 2 sleep on the stimulus delivery night. Consistent with results from the recording nights, individuals with a TBI had fewer evoked K-complexes than controls. This finding again suggests a breakdown

in sleep protective mechanisms. In contrast, no statistically significant group differences were found for either N550 latency or amplitude. One explanation may be that the K-complex is an all-or-none phenomenon, and its amplitude would therefore not be expected to vary among groups (Bastien & Campbell, 1992). Another, perhaps better, explanation is that the oddball paradigm used in this study was not optimal to evoke K-complexes. In fact, observation of the grand averages of the evoked K-complex for those with a TBI and their age-matched controls provides some evidence for the hypothesis that the N550 component was reduced in amplitude. The fact that the group difference did not reach statistical significance indicates that perhaps the stimuli used in this study were not salient or intrusive enough. Thus, employing a paradigm with more intrusive stimuli, such as an intensity oddball, or with more salient targets, such as rarer targets or one's own name, might be more useful in breaking through information processing gates to reveal group differences. Ideally, a paradigm designed to evoke K-complexes will deliver stimuli with a long, e.g., 30-second, inter-stimulus interval and an abrupt rise-fall time (Bastien & Campbell, 1992, 1994). Employing a paradigm with these considerations might allow researchers to demonstrate reductions in the N550 component in those with a TBI compared to good sleepers.

Individuals with a TBI were expected to have fewer and shorter spindles, indicating impairments in inhibition. Although greater injury severity was associated with reductions in spindle density, group comparisons showed that those with a TBI had more spindles and longer spindles. The night-to-night variability in these measures was also assessed. Consistent with hypotheses, participants with a TBI had more variability in both spindle density and duration, suggesting a dysregulation in sleep-protective mechanisms.

This instability in spindles may make it more difficult to reliably capture group differences in spindle activity. It should be noted that group differences were not highly robust, and observations were based on a combination of significant effects and trends. Thus, replication of these results would help to clarify the equivocal nature of the two types of analyses. Replication is especially important given that prior research has also yielded equivocal findings. Despite the need for replication, some explanation of the group differences can be offered. It is plausible that the increase in sleep spindle activity in those with a TBI represents a compensatory mechanism. Perhaps each spindle generated by an individual with a TBI represents less efficient inhibition than in good sleepers; thus, the nervous system compensates by increasing inhibitory activity, which is reflected in greater spindle activity. Also of note is the fact that the group differences in this study were limited to slow wave sleep. In good sleepers, there is a reciprocal relationship between spindle activity and depth of sleep (Dijk et al., 1993). Perhaps the group differences in this study indicate that the typical decline in spindle activity during slow wave sleep is impaired in TBI. Thus, greater spindle activity in those with a TBI might actually represent a maladaptive aspect of their sleep/wake regulation.

Power spectral analyses were computed on data in each sleep stage, on all three protocol nights. Quantitative EEG measures were used to demonstrate impairments in sleep homeostatic mechanisms, reflected in delta power, and the presence of hyperarousal, reflected in beta and gamma power. Individuals with a TBI were expected to have less delta sleep, reflecting disruption to sleep homeostatic mechanisms. In all non-rapid eye movement (NREM) sleep, those with a TBI had less delta power, consistent with predictions of impairments in homeostatic mechanisms. The time course

of the buildup of sleep pressure across the day and dissipation of sleep pressure through the night may be altered in those with a TBI. Impairments in the homeostatic system controlling the regulation of sleep and wakefulness may result in alterations in the depth of sleep and perhaps alterations in alertness levels through the day. These alterations would provide explanation for the trouble that individuals with a TBI have initiating and maintaining sleep, awakening adequately in the morning, and remaining alert through the day. Reduced delta power provides an explanation for complaints of non-restorative and non-efficient sleep. An interesting line of future research would be to use time-series analyses of delta power across the night to plot the delta power curve in those with a TBI to confirm these speculations. Second, a study designed to sleep deprive individuals with a TBI and then study their homeostatic recovery would provide further details regarding impairments in homeostatic sleep/wake regulation. In the same vein, studies investigating the effects of caffeine or other stimulants and those using napping paradigms would provide further information about sleep homeostatic mechanisms in TBI.

Those with a TBI were also expected to have more beta and gamma power, reflecting the presence of hyperarousal in sleep. Whereas there was evidence of more gamma power in Stage 2 sleep for those with a TBI, correlation analyses showed that greater injury severity was associated with lower gamma power. In slow wave sleep, those with a TBI had less gamma power than controls; correlation analyses supported that greater injury severity was associated with lower gamma power. Thus, hyperarousal may only be present in lighter sleep in those with a TBI; in deeper stages of sleep, other physiological mechanisms may override the breakdown in inhibition. In fact, in slow wave sleep, some compensation may occur to offset the hyperarousal in Stage 2 sleep.

Based on the idea that hyperarousal occurred in lighter sleep, it would be reasonable to consider that this hyperarousal exists in wakefulness as well. Results from data collected during wakefulness in this study showed that individuals with a TBI with complaints of insomnia had hyperarousal, i.e., greater beta and gamma power, in the pre-sleep waking period. This finding provides evidence for hyperarousal in a group of secondary insomniacs. In contrast, individuals with a TBI with daytime fatigue had less gamma power than their age-matched controls, demonstrating that qEEG findings reflected self-reported sleep complaints of those with a TBI. Further investigation of hyperarousal across the 24-hour day would be warranted. In addition to qEEG, recordings of metabolic and physiological variables may help to understand hyperarousal in this group.

Both a paired-click and a pitch oddball paradigm were delivered in NREM and REM sleep, as well as during pre- and post-sleep wakefulness. It was predicted that those with a TBI would show sensory gating and information processing impairments in wakefulness and sleep. Results for sensory gating in wakefulness confirmed hypotheses and previous research (Arciniegas et al., 1999, 2000, 2001; Arciniegas & Topkoff, 2004). In pre-sleep wakefulness, results for P50 amplitude to the second stimulus showed that those with a TBI had larger amplitudes than controls, suggesting poorer gating. In post-sleep wakefulness, those with a TBI had larger P50 suppression ratios. Both findings are consistent with predicted deficits in gating. As well, greater injury severity was correlated with a shorter P50 latency to both first and second stimuli, further evidence of heightened stimulus processing. In pre-sleep wakefulness, N1 amplitude, another measure of early encoding, was also larger to the second stimulus for those with a TBI, another finding consistent with predictions. However, post-sleep, N1 amplitude was smaller to both

stimuli, perhaps reflecting greater sleep inertia. ERP paradigms post-sleep on Night 3 were recorded immediately upon participants' awakening. Although this is standard practice in ERP research, it may not be surprising that sleep inertia was captured in the data. Overall, results from the paired-click paradigm in wakefulness were consistent with predictions.

In REM sleep, no group differences were found for P50 or N1 amplitude. The notion of hyperattentiveness was supported by the fact that individuals with a TBI had shorter P50 and N1 latencies. In Stage 2 sleep, the P50 peak could be identified despite a low signal-to-noise ratio, but few group differences were evident. Individuals with a TBI had a larger P50 amplitude, but smaller N1 amplitude, to the first stimulus. Overall, although impairments in sensory gating were observed in wakefulness, there were few group differences in sleep. White and Yee (1997) provided a systematic review of the parameters affecting elicitation and measurement of the P50 component. Altering some of these parameters, e.g., stimulus intensity, during sleep may provide more challenge to the sensory gating system, making group differences more apparent. Second, previous research documenting impairments in sensory gating in wakefulness in those with a TBI recruited only those with a TBI who experienced distractibility. Thus, perhaps using the paired-click paradigm in a similar group in sleep would demonstrate that impairments in sensory gating occur in sleep in those with complaints of attention problems. Finally, previous research using the paired-click paradigm in sleep has employed individuals with schizophrenia, because of a hypothesized relationship between the P50 component and acetylcholine function. These studies have manipulated sleep in order to manipulate acetylcholine levels. Thus, impairments in sensory gating in TBI may specifically be

linked to those with alterations in acetylcholine levels, such as individuals who have had damage to pontine or basal forebrain neurons.

During the oddball task, correlation analyses showed that greater injury severity was associated with slower and smaller ERPs in wakefulness. These findings are consistent with what is known from previous research (Lew et al., 2004; Rugg et al., 1993; Segalowitz et al., 2001; Solbakk et al., 1999, 2002). Group differences showed that those with a TBI experienced hyperattentiveness in wakefulness and Stage 2. In REM, correlation analyses showed that those with a TBI had slower and smaller N350 components, supporting the notion of sleep dysregulation. Importantly, while there were several pieces of evidence to support hypotheses, results were not robust, e.g., across sleep stage, across electrode site. Thus, using a more challenging oddball paradigm would be useful to break through the information processing gates of those with a TBI. Specifically, a basic pitch oddball was chosen due to the preliminary nature of the research. Using more biologically and/or psychologically salient stimuli would be more intrusive, and differences in the efficiency of the inhibitory system would become more obvious. As the first study using ERPs to investigate the sleep of individuals with TBI, the results found herein provide a solid basis for future research.

In general, results from sleep architecture, sleep phasic events, qEEG, and ERP analyses provided support for hypotheses that the sleep of individuals with a TBI can be characterized by impairments in inhibition, hyperarousal, and sleep/wake dysregulation.

Waking Performance Deficits and their Relationship with Sleep Physiology

Individuals with a TBI and age-matched controls were compared on neuropsychological, subjective, behavioural, quantitative EEG, and ERP measures during

wakefulness. Results confirmed predictions that those with a TBI had poorer cognitive and emotional functioning based on neuropsychological testing. Greater injury severity was associated with poorer performance on measures of attention, memory, and executive functioning, as well as with poorer adaptive functioning. Despite these widespread impairments in neuropsychological performance, few group differences were evident on laboratory-based computer tasks. The lack of group differences on measures of reaction time and accuracy does not suggest that those with a TBI perform as well as controls. Previous research (e.g., Asloun et al., 2008; Mathias, Beall et al., 2004; Rugg et al., 1993; Segalowitz et al., 2001) has well-documented that those with a TBI have impairments across a range of cognitive functioning. Instead, it is most likely that the tasks chosen in this study were not sensitive to the impairments typical of TBI. The tasks in the performance assessment battery were chosen for this study because of their known sensitivity to sleepiness, but may not have been sensitive to TBI. Thus, in future studies, different tasks might be investigated, or changes to task difficulty or length may also yield the expected outcomes. Because there is an inherent difficulty in repeating neuropsychological tests, particularly within the same study, the battery of neuropsychological tests in this study was chosen to measure participants' trait-like abilities, while laboratory-based testing was state-driven, i.e., it was thought that performance might vary from day to day, and from morning to evening. In future research, tasks will have to be carefully chosen to balance sensitivity to TBI with the ability to repeat tests at various times through the study.

As well, previous experimental research (Cote, Milner, Osip, Ray, & Baxter, 2003; Drummond et al., 2000; Drummond, Gillin, & Brown, 2001) on the effects of sleep

loss on waking function has shown that behavioural performance may remain intact, but compensatory neurophysiological processes are required for performance to be maintained. Thus, in this study, the TBI group may have been able to perform on task, but may have required additional compensatory neurophysiological processing, e.g., the recruitment of extra brain regions, additional gamma power reflecting neural effort. Future research utilizing more challenging paradigms would be able to provide information to this effect.

Those with a TBI and controls were also compared on a number of subjective variables, i.e., ratings of their sleepiness, mood, and sleep quality. Few results were found for mood variables. Significant effects indicated that the TBI group reported better moods than the control group, suggesting perhaps more interest in the study. Overall, those with a TBI reported poorer sleep, and those with more severe injuries reported greater sleepiness and fatigue. Importantly, individuals with a TBI with daytime fatigue reported more sleepiness and fatigue, and provided positive sleep quality ratings. Individuals with a TBI with insomnia, on the other hand, reported less sleepiness and fatigue, and rated their sleep more poorly than controls.

Power spectral analyses computed on data collected during the alpha attenuation task confirmed the dissociation between sleep complaint subgroups. Ratios of alpha power with eyes closed relative to eyes open and ratios of alpha to theta power were computed as indices of sleepiness. TBI participants with daytime fatigue had more EEG slowing and more physiological sleepiness. TBI participants with insomnia, however, had less physiological sleepiness than their controls. Correlation analyses showed that greater injury severity was associated with greater physiological sleepiness for high and total

alpha bands. As noted above, TBI participants with fatigue had less gamma power and those with insomnia had greater beta and gamma power. Thus, results from waking data were useful in illustrating the dissociation between sleep complaint subgroups. In future, researchers must therefore take this variable into account when investigating sleep and waking function in individuals with a TBI.

Event-related potentials were recorded during the Novel P3, n-back, and visual reaction time tasks. In summary, standard stimulus processing on both the Novel P3 and n-back tasks was faster and more efficient for those with a TBI. For target stimuli, there were no group differences for the n-back task; on the Novel P3 task, early encoding continued to be faster but a later P300 suggested impairments in attention. On the Novel P3 task, TBI participants with insomnia had larger N1 and P300 amplitudes, consistent with expectations of hyperattentiveness in this group, while those with fatigue had larger P2 amplitudes, suggesting greater inhibition, likely simply reflecting fatigue. No group differences were apparent for the ERN or Pe on the visual reaction time task. Because error monitoring depends on the functioning of the anterior cingulate cortex, alterations to the ERN and/or Pe were expected for those with a TBI. Thus, the lack of group differences in these measures likely resulted from the choice of task, e.g., not enough errors were committed, or errors were not noticed when they were made. Overall, previous research has shown impairments in information processing that were not replicated in this study. Given such consistent findings in previous literature showing that those with a TBI have impairments in information processing, the choice of alternate tasks may be necessary to illustrate these information processing deficits. Second, the results from this study have identified the need to consider TBI participants with

insomnia separately from those with fatigue. Thus, some of the null results may have resulted from collapsing across these groups, and therefore averaging across independent results for the two respective groups.

Finally, relationships between measures of sleep and waking function were investigated with a correlation approach in TBI and control groups. Many results confirmed hypotheses that poor sleep in the TBI group would be related to poor waking function, and that intact sleep in the control group would be related to intact waking function. Some results, however, were not meaningful in this way. For example, a number of results suggested that indices of efficient sleep were related to poor functioning; these relationships were often found for both groups. An overall consideration of these relationships suggested that deeper sleep was related to poorer functioning, which may be a reflection of sleep inertia. Performance assessment tasks took place at 09:00 h, in order to prevent sleep inertia. However, no studies have yet investigated whether sleep inertia persists longer in those with a TBI; this may be true particularly of those who complain of daytime fatigue. In addition, a lengthy break occurred before testing, during which time participants may have become groggy from boredom, producing symptoms similar to sleep inertia. Specifically, for the TBI group, poor sleep was related to poor performance and subjective ratings, and impaired sensory gating in sleep was related to poor performance, subjective ratings, and sensory gating during wakefulness. For controls, intact sleep architecture was related to intact information processing, but no other predicted relationships were found. Greater specificity with respect to the relationships between sleep and waking function is needed, particularly to direct treatment and to improve recovery.

Overall, neuropsychological test results confirmed deficits in cognitive and emotional functioning for the TBI group. Subjective and behavioural data collected in the laboratory provided limited support for hypotheses of subjective and cognitive deficits in TBI. Quantitative EEG measures of alertness were moderated by sleep complaint; individuals with insomnia had more alertness, while those with daytime fatigue had less alertness. Therefore, on many measures, it was important to consider sleep complaint subgroup to understand the nature of group differences. Results from behavioural and ERP analyses were limited and suggest that alternate tasks should be considered in future research.

General Discussion

Contributions. There were several design considerations that made this study a unique contribution to the literature. First, previous research on sleep and TBI has been limited to survey data and a scattering of polysomnographic and quantitative EEG studies. In the current study, a wide range of measures were utilized to study both the sleep and waking function of participants. The use of sleep architecture, phasic events, quantitative EEG, and ERPs allowed us to understand that the fragile sleep of individuals with a TBI can be characterized by impairments in inhibition and gating, the presence of hyperarousal, and homeostatic dysregulation. Second, this study employed a multiple-night design. The three protocol nights occurred on consecutive nights. This design was an advantage because it allowed us to explore night-to-night variability and helped to limit confounds, e.g., caffeine use or napping, that may have had more of an influence if nights occurred further apart. In addition, future studies would benefit from using a

similar design to analyze the impact of a good or bad night of sleep on waking function and the subsequent night's sleep.

As well, TBI participants were age-matched to the control group. This within-subjects design provided more power to the statistical analyses and prevented the influence of age from playing as great a role on the results. In addition, participants were rigorously screened to limit potential confounds to the data. Participants were required to be free of medications, non-smokers, and minimal caffeine users. Screening questionnaires were used to verify that participants' levels of stress, fatigue, and pain fell within a normal range. Finally, participants were required to be free of neurologic, cardiovascular, and psychiatric illness. Although the screening employed in this study may have limited the generalizability of the results, it was important to protect the internal validity of the study because it was a preliminary investigation.

As well, control participants were recruited to be healthy, good sleepers; no selection criteria were defined with respect to the sleep of individuals with a TBI. The final sample was comprised of individuals with complaints of insomnia, complaints of daytime fatigue, and no complaints about their sleep. This recruitment strategy was advantageous for this preliminary investigation because it allowed a broad investigation of how differences in sleep complaint moderated the results. For example, TBI participants with complaints of insomnia had greater physiological arousal, while TBI participants with complaints of fatigue had lower arousal levels. In the same way, individuals in the TBI group comprised all levels of injury severity, and thus an investigation of the impact of injury severity on the results was possible. For example, greater injury severities were associated with predicted reductions in spindle density,

illustrating that more severe injuries were related to greater impairments in inhibitory processes.

Limitations. One potential limitation of this study was the relatively small sample size. In each group, there were 20 participants. This number is sufficient for the within-subjects design, especially given the robust nature of many of the effects of interest, and is consistent with many other sleep studies. However, compared to many studies using survey data to examine sleep in TBI, this sample size falls short. There were a number of predicted results that suggest this sample size was sufficient; however, the trends ($p<.10$) in the data suggest that more power through a larger sample size would have helped to clarify results.

Second, one design consideration that may have been problematic was the length of time in the laboratory, especially in the morning. On recording nights, participants arrived at the laboratory at approximately 19:30 h (Night 1) or 20:00 h (Night 2), and were required to remain in the laboratory until 10:00 h. In the morning, participants were woken at 07:00 h and given free time until 09:00 h. This time period was designed to allow participants to rouse and eat breakfast, and for researchers to prepare participants, e.g., check electrode impedances, for the morning performance assessment battery. The length of the break and timing of the morning tasks were chosen to avoid capturing sleep inertia during testing, and to pair the testing time with the rise in circadian rhythms. However, anecdotally, participants felt that this break was too long, and became restless waiting for the tasks to begin. Ironically, they became fatigued due to boredom and thus morning tasks may have captured this amotivation. Evidence of this amotivation or

lingering sleep inertia was especially evident when examining relationships between sleep and waking function.

Finally, despite many findings that were consistent with predictions (e.g., changes to sleep architecture, reductions in K-complexes, reductions in delta power, impairments in sensory gating), there were a number of null results. The lack of predicted results with laboratory tasks, such as the Novel P3 task or pitch oddball task, was surprising. Previous research has confirmed that individuals with a TBI are impaired on cognitive tasks. However, in the current study, for the most part, no differences were found between those with a TBI and controls. These null findings may have been due to problems with the sensitivity and/or challenge in the tasks that were chosen. Tasks in this study were chosen to tap frontal lobe function, because frontal lobe function is often impaired both during periods of sleepiness and in TBI. However, tasks may not have been sensitive to the level of sleepiness of participants, or they may not have been sensitive to the degree or types of impairments of the TBI group. Although neuroimaging data were not available, participants in this study likely sustained damage typically witnessed with traumatic brain injuries, i.e., damage to frontal and anterior temporal lobes, damage to brainstem regions, diffuse axonal injury. Thus, while tasks were chosen to measure frontal lobe function, more complex tasks of the same nature may have been needed to capture deficits. Additionally, variability in the TBI group may have masked group differences from a statistical standpoint.

Future considerations. First, given that this is a preliminary study, it is important to replicate these findings. Examination of these quantitative electrophysiological variables, along with cognitive function, in a larger sample would be prudent. In addition,

participants in this study were recruited to be free of disorders and medication-free, but were not limited in terms of injury severity or sleep problem. Based on data from the current study, it is clear that future research should investigate sleep in larger and more homogeneous samples of participants with a TBI. For instance, it would be a logical next step to study sleep in a large group of TBI participants with complaints of insomnia. This study could compare a TBI group to a group of psychophysiological insomniacs to determine if markers of sleep regulation and hyperarousal were impaired to the same extent and in the same way in both groups. Future research should also investigate sleep in participants with a TBI who have similar injury severities, e.g., all moderate to severe injuries. Although a more clinical approach to participant recruitment would be appreciated by researchers and clinicians, a greater understanding of basic sleep physiology and its connection to waking function in this group is needed first. Therefore, research must continue to employ samples of TBI participants who are free from conditions that might confound interpretation.

In contrast, because it is rare that individuals who have sustained a TBI are free of any comorbid difficulties (e.g., emotional dysregulation, headache, chronic pain), a more general sample would allow results to be applied to a wider population. Thus, future researchers could examine a more general sample of participants to increase the external validity of results. A large epidemiological study could be undertaken to study the sleep and waking function of those with TBI. With this approach, regression strategies would be used to statistically evaluate the amount of variance accounted for by a range of participant characteristics, health status, lifestyle factors, and comorbidities.

A goal of this study was to investigate the relationship between sleep disruption and waking function. Individuals with TBI often complain of problems with memory. A "hot topic" in sleep research currently is the role of sleep in learning and memory. Given the advances that have been made in this field in recent years, there is now more understanding about the changes to sleep neurophysiology that occur in response to learning. Thus, future researchers could draw upon this new knowledge to determine whether the learning impairments seen in TBI could be attributed to a lack of consolidation during sleep. This may be done through sleep deprivation paradigms that investigate how specific types of learning are impaired by disruption of specific sleep stages. The alternative design is to investigate how learning new information is consolidated in sleep, e.g., by changes to sleep spindles or REM density in sleep periods following learning. This knowledge may help to direct treatment in terms of developing appropriate compensatory strategies and memory aids. Specifically, it may be prudent to treat the sleep difficulties of those with a TBI before engaging in cognitive-behavioural therapy, so that these individuals can maximize benefits of such rehabilitation strategies.

Individuals with TBI and their treatment providers have an interest in this type of research because they are hopeful that it can provide treatment directions. Sleep disruption is a salient problem for many individuals with TBI for a number of reasons, including disruptions to cognitive and emotional functioning in response to poor sleep, and including difficulty making gains in therapy due to poor sleep. Thus, research that could directly improve sleep would be useful in helping these individuals make further recovery in other domains of functioning. Therefore, future research with a treatment component would be useful in a variety of ways. Based on the current research,

psychological and/or pharmacological treatments could be developed, e.g., to enhance the depth and character of sleep to make it more efficient; future research could then use these treatments with individuals with a TBI and study the outcome on both their sleep physiology and their waking function.

In summary, based on considerations of the results of this thesis, contributions based on the study design, and limitations to the study, there are several specific areas of future research that would add to the literatures on sleep and traumatic brain injury. First, using different ERP paradigms would help researchers to better understand information processing during sleep in TBI. The use of different tasks would also allow researchers to better grasp the relationship between sleep and waking function. A particular line of research may be to investigate the relationship between sleep and memory in TBI. Researchers also need to further investigate sleep spindles in TBI to determine if they are better conceptualized as markers of compensation or dysregulation. Researchers can use challenge paradigms (e.g., sleep deprivation, stimulant dosing paradigms) to further investigate homeostatic mechanisms in TBI. Investigating hyperarousal across the 24-hour day can be accomplished with metabolic and physiological measures. Finally, using more homogeneous samples and/or larger samples that would allow the investigation of a wide range of variables is key to future research.

Conclusion. In summary, this study used a variety of measures of sleep physiology (sleep architecture, sleep phasic events, quantitative EEG, ERPs) to compare those with a TBI and age-matched controls. Results suggested that the sleep of those with a TBI was lighter and less efficient, as measured by sleep architecture variables. As well, there was a clear decline in the generation of spontaneous and evoked K-complexes in

TBI. Results for sleep spindles showed that injury severity predicted a decline in spindle density, though spindles in slow wave sleep were longer for individuals with a TBI than for controls. Quantitative EEG showed that sleep homeostatic mechanisms were impaired in TBI, while ERPs suggested that participants with a TBI experienced impairments in sensory gating, particularly in the pre-sleep waking period. Both quantitative measures supported the notion that individuals with a TBI showed evidence of hyperarousal. While neuropsychological testing and subjective data confirmed predicted deficits in the waking function of those with a TBI, group differences were not found on laboratory computer-based tasks. Finally, a number of correlations supported the hypothesized relationship between sleep impairment and waking deficits in those with a TBI. In future, researchers should consider the need for a systematic and comprehensive investigation of the sleep of those with a TBI, the impact of sleep complaint and injury severity, and the possibility of alternate performance assessment tasks, in order to better understand the neurophysiological underpinnings of changes to sleep that occur in individuals with a TBI.

Overall, this thesis provided evidence that the fragile sleep seen after a TBI is due to a number of related mechanisms. TBI is characterized by damage to predictable areas of the brain (i.e., brainstem, hypothalamus, cortex, white matter), due to typical acceleration/deceleration and rotational forces involved in the event. Given these predictable regions of damage, it is no surprise that sleep and wakefulness are disrupted after a TBI, particularly given the widespread regions of the brain controlling these functions (e.g., reticular activating system, pons, medulla, hypothalamus, thalamus, cortex). Trauma to cortical, subcortical, and brainstem regions that regulate sleep and

wakefulness may affect sleep/wake homeostasis, disrupt the brain's ability to efficiently gate irrelevant information, and allow for the presence of hyperarousal. The results from this thesis help to understand the nature and extent of sleep complaints in TBI, versus other neurological, medical, and psychiatric disorders. Many of the regions of the brain that control sleep and wakefulness are vulnerable to damage with TBI, and the results of this study support the idea that systems controlling the brain's ability to regulate the depth and quality of sleep, inhibit irrelevant information, and maintain the appropriate level of arousal are specifically damaged in TBI. The same type of fragile sleep would not be expected in other disorders, where there is damage or dysfunction in other regions of the brain.

Moreover, the results of this study pointed to the importance of taking the self-reported sleep complaints of participants into account. A dissociation between TBI participants with insomnia and those with fatigue was evident on multiple variables. Thus, the mechanisms responsible for these two distinct presentations may also be quite distinct. Specifically, individuals with a TBI who complain about insomnia may have disruptions in brainstem regions controlling arousal (i.e., they remain hyperaroused through the night), or they may have impairments in thalamocortical inhibitory processes that serve to protect the sleeping brain from intrusions from irrelevant stimuli. Although reductions in K-complexes and delta power were different than what would be expected for psychophysiological insomnia, the presence of hyperarousal is consistent with primary insomnia. In contrast, individuals with complaints of fatigue likely have damage to hypothalamic regions, causing disruption to hypocretin neurons and therefore reductions in arousal level. Recent research showing that a proportion of TBI survivors

have reductions in hypocretin levels even six months post-injury (Baumann et al., 2007) suggests that this mechanism may be responsible for complaints of fatigue following TBI.

In summary, this thesis provides a first step toward understanding the mechanisms that contribute to the fragile sleep seen after a TBI and will allow future researchers to understand how these mechanisms differ from other medical disorders that are characterized by changes to sleep. Finally, the importance of differentiating individuals with a TBI with insomnia from those with fatigue was an important aspect of this project, and is supported by recent neurobiological and ERP research.

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Sensory gating impairments in poor sleepers during presleep wakefulness

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The neurocognitive model of insomnia predicts information processing deficits in poor sleepers. There is some evidence for deficits in later cognitive processing, but earlier sensory processing remains to be investigated. Paired-click stimuli were delivered to good and poor sleepers in a single night. P50 amplitude to stimuli provided an index of sensory gating in presleep wake, rapid eye movement sleep and stage 2 sleep. Poor sleepers exhibited sensory gating impairments during wake. For both groups, gating was intact in rapid eye movement sleep but absent in stage 2 sleep. These data show that poor sleepers experience enhanced sensory processing in the waking period before sleep. Further study is needed to explore sensory gating in chronic primary insomnia, sleep maintenance insomnia, and across multiple recording nights. *NeuroReport* **20:331–336 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Introduction

Insomnia is a sleep disorder characterized by difficulty in falling asleep or staying asleep [1]. It is a highly prevalent disorder with negative consequences for safety, productivity, and well-being. Several models have been put forth to explain the aetiology and pathophysiology of the disorder [2]. Early work identified physiological indices that were elevated in patients with insomnia (e.g. heart rate). A behavioural model of insomnia suggests that insomnia develops from the interaction of precipitating and predisposing factors, followed by maladaptive coping strategies that perpetuate the insomnia [3]. Cognitive aspects of the disorder are evidenced by consistent reports of excessive rumination and worry at bedtime. The neurocognitive model identifies conditioned central nervous system arousal as a factor in the development and persistence of insomnia [4]. In support of this, high-frequency electroencephalogram activity (e.g. beta/gamma) is greater in patients with insomnia compared with good sleepers at sleep onset and in sleep. The model also predicts that central nervous system activation will correspond to enhanced sensory and information processing, and increased long-term memory. In an investigation of verbal memory at sleep onset [5], poor sleepers recognized significantly more words during sleep onset compared with good sleepers, suggesting that they have heightened processing at sleep onset. The use of event-related potentials (ERPs), however, would provide a more direct measure of sensory and cognitive processing in insomnia.

ERPs are recorded using scalp electrodes and consist of waveforms that represent the brain's processing of stimuli [6]. The long-latency ERP waves elicited to auditory stimuli are referred to as 'P1', 'N1', 'P2' and 'P300' to reflect their polarity, order, and latency. These peaks represent various stages of information processing: P1 at 50–75 ms reflects early sensory processing, N1 at 80–100 ms represents encoding of stimulus, and P2 at 175–225 ms has been linked to a process of inhibition [7]. The later P300, peaking around 300 ms, represents more complex cognitive processing, such as stimulus discrimination, target identification, and possibly memory updating [6]. N1, P2, and P300 vary predictably with changing levels of arousal and depth of sleep [8,9]. In healthy, good sleepers, N1 decreases and P2 increases at sleep onset. P300 disappears in late stage 1 when the sleeper no longer provides a behavioural response. The earliest of the long-latency components, P1, has been described in good sleepers, but the findings are mixed, with some reporting P1 increases in amplitude, but others reporting that it decreases during sleep [10]. The changes to N1, P2, and P300 have been well described in healthy, good sleepers, but little work has been done applying ERP techniques to the problem of insomnia.

Two recent studies found that P300 was larger in poor sleepers than good sleepers in wake when a poor night of sleep was reported [11,12]. This waking hyperarousal in poor sleepers is consistent with the neurocognitive model, but only provides evidence for deficits in later stages of cognitive processing (e.g. target detection). One study reported differences between good and poor sleepers on earlier components [13], N1-P2, during the first 5 min of stage 2 sleep. Poor sleepers had larger N1

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and smaller P2 peaks, which is consistent with a state of hypearousal or attentiveness. Poor sleepers also had a smaller N350 amplitude, which is a sleep-specific waveform associated with inhibition during sleep. These data are preliminary as only a single recording of 5 min of stage 2 was investigated, and evoked K-complexes were not removed from the analysis. A more recent study also investigated the early components during wake and a single sleep onset period [14]. The authors reported that poor sleepers had a larger N1 during both presleep and postsleep wake, indicating that poor sleepers were hyperattentive in the waking state. In the analysis of the sleep onset period, K-complexes were removed, but a smaller N1 and larger P2 was observed in poor sleepers, which contradicts the previous report [13]. Results were concordant, however, for the N350 that was smaller for poor sleepers and consistent with the notion of hyperarousal. Both studies had very few trials available for reliable ERP averaging from a single sleep onset period, and they investigated different physiological states (e.g. stage 2 only [13] vs. wake through to the onset of stage 2 [14]), making conclusions difficult. More work is needed in this area to characterize the nature of information processing deficits in poor sleepers.

Another way to investigate early sensory processing is through the use of the so-called paired-click paradigm, which elicits the P50 mid-latency component. This paradigm is ideal for investigating sensory gating in particular, and has not been reported previously in poor sleepers. Maximal at the vertex, the P50 is most likely generated by a widespread cortical area under the control of the primary auditory cortex [15]. A gradual decrease in P50 amplitude as the interstimulus interval of stimuli increases (e.g. >1 per second) has been reported [16]. On the basis of this, sensory gating is measured using the paired-click paradigm where two clicks are presented in rapid succession. The first click is reliably attended to, whereas the second click is considered less relevant and not processed further [17,18]. If the two stimuli are processed to the same extent, it reflects failure to inhibit irrelevant information at the sensory level.

The P50 paradigm has been well studied in patients with schizophrenia as a marker of their sensory gating abnormalities [19–22]. Two studies have measured P50 using the paired-click paradigm during sleep [21,22]. First, sensory gating was recorded in wake and rapid eye movement sleep (REM) in healthy, good sleepers [21]. Results from non-REM (NREM) sleep were inconsistent, that is, suppression of P50 improved for some but worsened or was not detected for others. Given these equivocal results and the fact that some of the participants in this study failed to suppress in the waking state, no conclusions can be made about sensory gating in NREM sleep. In a subsequent study in schizophrenics [22], it was found that healthy controls exhibited appropriate P50 suppression in both wake and REM, whereas schizophrenics showed sensory gating deficits in both states. NREM data were not reported.

In this study, the paired-click paradigm was applied to investigate sensory gating abnormalities in poor sleepers compared with good sleepers. It was hypothesized that poor sleepers would show impairments in sensory gating during wakefulness. On the basis of previous research [22], it was expected that sensory gating deficits would also be apparent in REM sleep. Although no prior research exists to predict effects in NREM sleep, it was expected that utilizing appropriate analysis techniques (i.e. removing K-complexes), and recording from a sufficient number of trials, would allow for investigation of sensory gating impairments in poor sleepers in stage 2 sleep.

Method

Participants

Good and poor sleepers were recruited from a university setting to spend a single night in the sleep research laboratory. Inclusion criteria required that all participants be nonsmokers in good health, taking no medications, with no history of chronic pain, neurological problems, heart disease, or mood/psychiatric disorders (no personal or family history of schizophrenia). Both good and poor sleepers had regular sleep/wake schedules, did not work in shifts, and were not phase-delayed. Good sleepers had no history of sleep disorders. Poor sleepers reported either trouble falling asleep or staying asleep, and the problem must have occurred on at least three nights per week, for at least 1 month. Poor sleepers must also have indicated that their sleep difficulties interfered with their daytime functioning and/or alertness. Twenty-nine participants completed the overnight. Three people were subsequently removed from all analyses because of the presence of periodic limb movements. The final sample included 13 good sleepers (mean age = 22.23 years, SD = 2.45, five males) and 13 poor sleepers (mean age = 20.38 years, SD = 2.57, four males).

Procedure

In a telephone interview, candidates were asked about sleep habits and health. Eligible participants spent one night (20:00–08:00 h) in the laboratory. Participants gave informed consent and completed questionnaires to verify inclusion criteria (e.g. sleep, circadian rhythms, health, mood). Participants completed an inventory to assess stress level [23] because stress has been reported to modulate recording of the P50 [24]. Participants completed a hearing test to verify that hearing was within normal range.

After electrode application, at 22:30 h, a 30-min paired-click paradigm was delivered through earphones, using STIM software (Compumedics Neuroscan Inc., El Paso,

Texas, USA). Participants sat upright at a computer in a private bedroom and had a break every 10 min. They were instructed to look at a fixation point located in the middle of the screen, and to listen to the clicks but not to respond. They were also asked to minimize blinking and movement. After completing a presleep questionnaire, lights were turned out and bedtime occurred at 23:00 h. No stimuli were delivered during the sleep onset period. After 5 min of consolidated stage 2 sleep, defined by the presence of K-complexes and/or spindles, stimulus delivery began and continued until 07:00 h. Upon awakening, participants completed a postsleep questionnaire and a 30-min paired-click paradigm was administered. Participants received a $20 honorarium or earned research hours for university courses. Procedures were cleared by the local research ethics board.

Electrophysiological recording and analysis

Standard clinical polysomnography recorded with SCAN software (Compumedics Neuroscan Inc.) verified that participants were free from respiratory and movement-related sleep disorders. An electroencephalogram (EEG) was recorded at midline scalp sites (Fz, Cz, Pz) and central sites (C3, C4), referenced to FPz and grounded to AFz. A horizontal electrooculogram (EOG) was recorded from the outer canthus of each eye. A vertical electrooculogram (EOG) was recorded from above and below the right eye. An electromyogram (EMG) was recorded submentally. Data were sampled at 1000 Hz (DC to 100 Hz filter applied).

Parameters for the ERP paradigm were derived from previous research [24]. Two 0.04 ms square-wave clicks were delivered binaurally at 95 dB SPL (clicks are low frequency and short duration, therefore not disturbing sleep), with a constant interstimulus interval of 500 ms. An intertrial interval was held constant at 10 s.

Sleep stages were scored according to standard criteria [25], except that stage changes were marked at the precise moment of their occurrence, as opposed to the end of each 30 s epoch. This scoring technique is necessary to assure that each stimulus is appropriately binned with the correct sleep state, and has been applied in previous ERP studies of sleep [26].

ERP averages were stimulus locked, with a total sweep time of −100 to 900 ms. During wake, trials containing eye blinks or movement artifact were rejected from the average. During stage 2 sleep, trials containing K-complexes or movement artifact were removed. Averages were computed for the first and second click separately, for wake, stage 2, and REM. Waking data from the morning was not analysed further because a sufficient number of trials could not be obtained as a result of excessive blink and movement artefact. The mean number of trials per participant, for each stimulus type, was 70 in presleep wake, 168 in REM, and 178 in stage 2.

P50 and N1 waveforms were identified at Cz. Based on earlier studies [21,22,24], P50 to the first click was defined as the most positive peak 40–80 ms after the stimulus. Peak-to-peak measurements were calculated from the preceding negative peak. The larger amplitude N1 was used as a guide to locate P50 latency. P50 to the second click was identified within 10 ms of its latency to the first click. Suppression ratios for P50 were calculated (stimulus2 : stimulus1) on the individual data as a measure of sensory gating. A 10–50 Hz bandpass display filter was used during a 125 ms sweep (0–125 ms). Baseline-to-peak amplitude measurements of N1 were obtained as another measure of early sensory processing. N1 was defined as the most negative peak after stimulus presentation in a 300 ms sweep (−100 to 200 ms) using a 30 Hz low-pass display filter.

Data analysis

All data were analysed with group (good, poor sleepers) by stimulus type (first, second click) analyses of variance. Significant interactions were followed with paired *t*-tests to determine the amount of suppression in each group. A ratio of P50 amplitude (second click/first click) was also computed to compare the level of suppression between groups. One good sleeper and one poor sleeper were missing from the data analysis for wake because of technical problems. No outliers were identified.

Results

All poor sleepers reported frequent difficulty falling asleep, and four also experienced sleep maintenance problems. Their mean Insomnia Severity Index was 12.0 (SD = 4.7; range = 5–19), which falls in the subthreshold category of severity [27]. In the laboratory, poor sleepers took significantly longer to fall asleep [poor: $M = 17.94$ min, SD = 6.94; good: $M = 9.23$ min, SD = 4.40, $t(24) = -3.82$, $P < 0.001$], but did not differ on sleep efficiency [poor: $M = 84.99\%$, SD = 7.78; good: $M = 87.64\%$, SD = 5.98, $t(24) = 0.97$, NS]. Groups did not differ statistically on their level of stress, although the good sleeper group met the norm for a student population (PSQ index = 0.36 [23]), and the poor sleeper group exceeded it (mean PSQ index = 0.49).

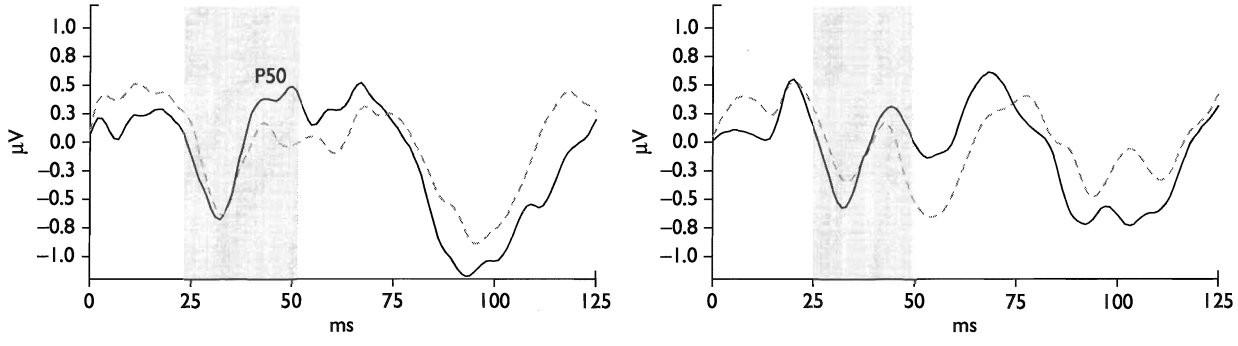
The amplitude and latency data for both P50 and N1 waveforms are presented in Table 1. The P50 waveform was visible in all stages in each individual average. Mean latency of P50 did not differ between groups in wake, REM or stage 2 sleep. Examination of the grand average waveforms for each group illustrated that poor sleepers had less P50 suppression in wake compared with good sleepers (Fig. 1). The group by stimulus type interaction for P50 amplitude was marginally significant,

Table 1 Means and standard deviations for P50 and N1 amplitude and latency in all stages

		P50		N1	
		Good sleepers	Poor sleepers	Good sleepers	Poor sleepers
		M (SD)	*M* (SD)	*M* (SD)	*M* (SD)
Amplitude (μV)					
Wake	Stimulus 1	2.26 (0.75)[a]	2.17 (1.16)	−2.48 (2.38)	−1.84 (1.87)
	Stimulus 2	0.92 (0.84)[a]	1.57 (0.85)	−1.35 (1.31)	−1.56 (1.11)
	Ratio	0.38 (0.28)[b]	0.81 (0.58)[b]	0.65 (1.12)	−2.41 (10.91)
REM	Stimulus 1	0.86 (0.40)	1.05 (0.80)	−0.83 (0.79)	−0.70 (1.13)
	Stimulus 2	0.66 (0.41)	0.59 (0.45)	0.02 (0.79)	−0.59 (1.15)
	Ratio	0.79 (0.47)	1.17 (1.76)	4.97 (17.00)	−1.99 (12.33)
Stage 2	Stimulus 1	0.56 (0.36)	0.75 (0.49)	0.33 (0.91)	0.85 (0.80)
	Stimulus 2	0.52 (0.32)	0.85 (0.57)	0.95 (1.28)	0.53 (1.16)
	Ratio	1.12 (0.83)	1.97 (3.21)	−1.10 (2.87)	0.39 (3.52)
Latency (ms)					
Wake	Stimulus 1	58.50 (12.30)	65.75 (12.59)	113.42 (13.42)	108.83 (12.78)
	Stimulus 2	56.58 (10.82)	65.67 (13.23)	111.00 (11.95)	105.67 (16.30)
REM	Stimulus 1	65.23 (11.55)	60.00 (10.89)	111.92 (17.59)	116.62 (14.15)
	Stimulus 2	64.85 (13.58)	62.62 (14.17)	106.08 (16.62)	110.23 (11.69)
Stage 2	Stimulus 1	52.31 (9.50)	55.31 (11.64)	109.77 (13.92)	99.69 (13.05)
	Stimulus 2	49.92 (7.61)	55.54 (13.70)	105.69 (12.94)	97.77 (16.32)

REM, rapid eye movement sleep.
[a]Indicates a significant difference between stimulus 1 and stimulus 2 in wake.
[b]Indicates a significant difference between good and poor sleepers for the ratio (S2 : S1) in wake.

Fig. 1



Grand average waveforms during presleep wakefulness. Event-related potential (ERP) waveforms representing differences in P50 amplitude between good sleepers (left) and poor sleepers (right) during presleep wakefulness. The solid line represents the ERP to the first stimulus and the dashed line represents the ERP to the second stimulus. The amplitude of the P50 peak to the preceding negative peak is highlighted in grey. Note that good sleepers had greater suppression to the second stimulus, relative to the first, compared with poor sleepers.

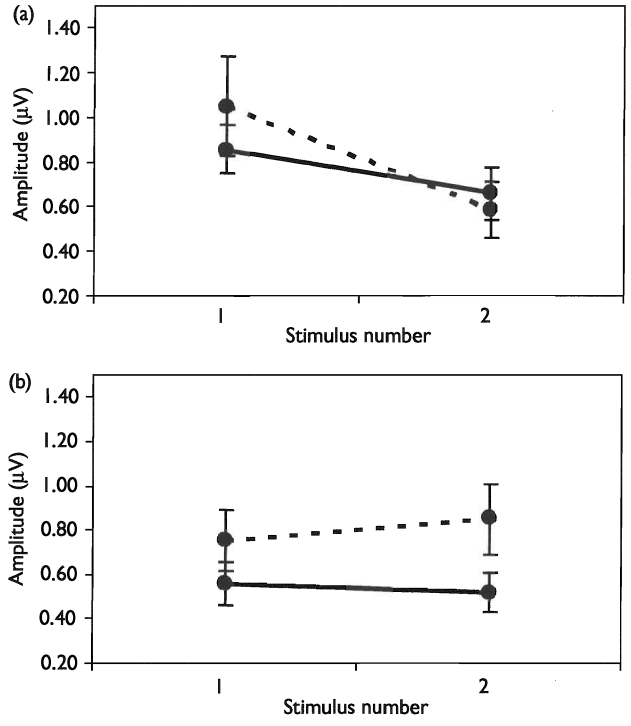
$F(1,22) = 4.23$, $P = 0.052$. Paired *t*-tests were then run to examine the degree of suppression in each group. The *t*-test for good sleepers confirmed that the decrease in sensory processing, from the first stimulus to the second, was highly significant, $t(11) = 6.67$, $P < 0.001$. Furthermore, as predicted, the *t*-test for poor sleepers confirmed deficits in sensory gating, such that poor sleepers did not significantly suppress their response to the second click, $t(11) = 1.95$, $P = 0.078$.

To further investigate this effect, a ratio of P50 amplitude (second click/first click) was calculated for each group. A two-tailed independent-samples *t*-test confirmed that poor sleepers ($M = 0.81$, $SD = 0.58$) had impaired sensory gating relative to good sleepers ($M = 0.38$, $SD = 0.28$), $t(22) = 2.31$, $P = 0.03$.

In REM, there was an effect of stimulus type illustrating that both groups suppressed their response to the second stimulus, $F(1,24) = 8.337$, $P = 0.008$. There was no significant interaction. Although P50 was identified in the grand and individual averages in stage 2 sleep, there was neither a stimulus type effect, nor a group by stimulus type interaction, suggesting that sensory gating as indexed by the P50 could not be observed in stage 2 sleep (see Table 1 and Fig. 2).

N1 was examined as a measure of early sensory processing and encoding. Group by stimulus type analyses of variance yielded no significant results for N1 amplitude in wake or sleep (Table 1). However, in REM sleep, there was a main effect of stimulus type for N1 latency, $F(1,24) = 7.56$, $P = 0.011$, where the second stimulus was

Fig. 2



P50 amplitude to paired-click stimuli in sleep. (a) Interaction plot of P50 amplitude to paired-click stimuli during rapid eye movement sleep (REM). Both groups suppressed their response to the second stimulus, relative to the first, in REM. (b) Interaction plot of P50 amplitude to paired-click stimuli during stage 2 sleep. Solid lines represent the good sleepers and dashed lines represent the poor sleepers. Error bars represent the standard error of mean.

processed more quickly than the first stimulus for both groups. In stage 2, there was a trend for a group effect, $F(1,24) = 3.98$, $P = 0.057$, indicating that poor sleepers tended to process both types of stimuli more quickly than good sleepers.

Discussion

Sensory gating in good and poor sleepers was investigated during a single night in the laboratory. Presumably, good sleepers can initiate and maintain sleep by disengaging from the environment in an automatic and effortless manner and can successfully gate irrelevant stimuli. The neurocognitive model of insomnia suggests that conditioned arousal creates an inability to attenuate cortical processing during wake and sleep [4]. Therefore, it was hypothesized that impaired sensory gating, indexed by the P50, would be a fundamental characteristic of poor sleepers during both wake and sleep. Our data provide evidence that poor sleepers experience deficits in sensory gating during presleep wake.

Both good and poor sleepers showed evidence of sensory gating during REM sleep, but no group differences in the degree of suppression were observed. It is possible that sensory gating deficits were not apparent in REM sleep in this particular sample, because poor sleepers reported predominant sleep onset difficulties. In stage 2 sleep, the P50 could be identified in the waveforms for all participants, but there was no evidence of a suppressed response to the second click for either group. It is likely that NREM sleep represents a time in which sensory processing is considerably blocked altogether.

These young, self-reported poor sleepers are not likely the same as chronic primary insomniacs whose conditioned arousal has persisted over a long period of time. Furthermore, our finding of sensory gating deficits being restricted to the waking period may coincide with the subtype (sleep onset) of insomnia investigated here. It would be prudent for future research to investigate more severe or long-term cases of primary insomnia, and to explore the timing of sensory gating deficits in various subtypes of insomnia (e.g. sleep maintenance groups).

Furthermore, future research should examine both a good and poor night in each participant. It may be that information-processing deficits occur only on bad nights (as suggested by data on P300 [11,12]). A number of other variables likely influence the extent to which poor sleepers will show impaired information processing. Researchers need to investigate the relationship between ERPs and quality of sleep, level of sleepiness, stress level, and mood to understand the variability in the data. Further, recording from participants over multiple nights would allow them to better acclimatize to the laboratory environment, and would avoid the possibility of capturing a so-called reverse first night effect (where poor sleepers sleep better away from home).

Conclusion

The current research is novel in investigating sensory gating in poor sleepers during wakefulness, REM, and NREM sleep. Deficits in sensory gating were found in poor sleepers during presleep wake, but were not observed in sleep. Sensory gating was apparent in REM sleep, but did not differ between the groups. The sample was comprised of individuals with predominant sleep onset difficulties, and thus it is plausible that differences in sensory processing existed at bedtime but did not persist during sleep. This outcome is consistent with the neurocognitive model insomnia [4], in that patients with sleep onset difficulties experience heightened sensory processing before sleep. This impaired gating in wakefulness may explain sleep perception problems that are characteristic of insomnia, such as inability to accurately judge sleep onset latency.

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INCLUSION/EXCLUSION CRITERIA	
AGE	18-65 years old
SLEEP	Normal schedule; no shift work; no sleep disorders (comorbid insomnia for TBIs permitted)
MEDICATIONS	None
CAFFEINE USE	Minimal use
SMOKING STATUS	Non-smoker
MEDICAL HISTORY	No neurological, cardiovascular, or psychiatric illness (comorbid depression/anxiety for TBIs permitted)
PERCEIVED STRESS	Normal range (higher for TBIs permitted)
FATIGUE	Normal range (higher for TBIs permitted)
PAIN	None (mild pain for TBIs permitted)

Name:	Date:

I. DESCRIBE STUDY:

We are interested in studying the sleep physiology of individuals with traumatic brain injuries, and those without. To this end, we will ask that you visit the Sleep Lab at Brock on a number of occasions. First, we will schedule you in for an orientation session, which will take approximately 1 to 2 hours. During this session, we will show you the lab and our equipment, have you complete a questionnaire package, complete a hearing test, and practice several computer tasks. Next, we will have you stay in the lab overnight for one night before the study starts. This night will verify that you do not have any sleep disorders. On this night, you will again be asked to practice the same computer tasks. In the morning, you will be sent home with a sleep and activity diary, to record your sleep for a week. Finally, before the study begins, we will have you come back to the laboratory for approximately a half a day, during which we will administer a number of neuropsychological tests. Unfortunately, the results of these tests are only for research and we will not be able to provide you with any individual information.

For the main part of the study, we'll ask you to come to the Sleep Lab on consecutive nights. You will need to arrive at approximately 8:00 p.m. each night and you will be able to leave in the morning at approximately 10:00 a.m. At home, we ask that you continue your sleep and activity diary. When you arrive at the lab, you will have electrodes applied to your scalp and face. Following this, you will be asked to complete a number of tests on computer. You will also repeat these tests in the morning. On the first and second nights, you will be allowed to sleep uninterrupted. On the third night, tones will be played throughout the night while you sleep. These are not intended to wake you up, but merely to assess how your brain processes information in the environment while you are asleep. We will also ask that you do not nap, drink caffeine, smoke, or drink alcohol for the three days prior to the nights you spend in the lab. You will be given an honorarium of $125 for your time.

II. INCLUSION / EXCLUSION CRITERIA (GENERAL):

Sex: M / F [circle one]

Have you sustained a traumatic brain injury? Y / N [circle one]

If Yes: Was this your first brain injury? [yes]: _____

When did your injury occur? [at least 6 months ago]: _____

Did you go to the hospital or the doctor? [yes]: _____

Did you require surgery or have to stay in the hospital due to complications? [no to surgery and no to infection]: _____

Do you use a wheelchair or other assistive device? [no]: _____

Do you have trouble communicating with others due to your injury? [no]:_

Age: _____

Weight: _____ Height: _____

Right or left handed: _____

English as first language [yes]: _____

Smoking status [able to be in lab without cigarette]: _____

Napping status [able to go without napping during the study protocol]: _____

How many caffeinated drinks do you typically have in a day [less than 3]: _____

III. SLEEP:

1. Do you consider yourself a good sleeper? [yes for controls]

2. What are your usual sleeping times (e.g., bed and rise times)? [approx. 11:00 to 7:00]

3. Do you have any history of shift work? [no]

4. Do you have difficulty falling asleep at night? [no for controls]

5. Do you wake up often during the night and are unable to return to sleep? [no for controls]

6. Do you wake up earlier than you would like in the morning and are unable to return to sleep? [no for controls]

7. Would you describe yourself as excessively tired during the day? [no for controls]

8. Have you ever been diagnosed with a sleep disorder? [no, comorbid insomnia ok for TBIs]

IV. HEALTH:

1. Are you presently in good health? [yes]

2. Are you taking any medication? [no for controls; no to anti-psychotics, narcotics, stimulants, hypnotics for TBIs]

3. Do you suffer from chronic pain, such as arthritis or fibromyalgia, or soft tissue injury? [some pain ok]

4. Do you have any history of or suffer from any neuropathological condition, such as MS, previous brain injury, or brain tumour? [no]

5. Do you suffer from epilepsy or other neurologic illnesses? [no]

6. Do you have any history of heart disease or stroke? [no]

7. Do you suffer from depression or anxiety? [no for controls, no pre-morbid for TBIs]

8. Do you or does anyone in your immediate family suffer from schizophrenia? [no]

TBI Group	Control Group
▸ *n* = 20 (9 males)	▸ *n* = 20 (10 males)
▸ *Mean age* = 29.75 (*SD* = 14.17)	▸ *Mean age* = 29.40 (*SD* = 13.68) *age-matched to TBIs
▸ Sleep complaints: 1. insomnia (*n* = 10) 2. fatigue (*n* = 6) 3. none (*n* = 4)	▸ No sleep complaints
▸ Injury severity: 1. mild (*n* = 6) 2. moderate (*n* = 8) 3. severe (*n* = 6)	▸ No history of head injury

SLEEP - WAKE QUESTIONNAIRE

ID	DATE (dd/mm/yy)	HEIGHT	WEIGHT	SEX

INSTRUCTIONS

Read each of the questions carefully and select a scale number that best describes HOW OFTEN YOU HAVE HAD THESE DURING THE PAST **2 MONTHS**. Place the number in the block immediately to the right of the item.
Do not skip any item and print your numbers clearly. Make sure that you have answered all the questions.

SCALE

0 Never **2 Sometimes** **4 Always**
1 Rarely **3 Often** **5 N/A**

EXAMPLE

How often do you awaken more than 5 times at night?

Answer:..... [3]

(This means that you **often** awaken more than 5 times at night)

1 **Before going to sleep how often do you engage in the following activities:**
a) Read .....
b) Smoke .....
c) Eat a snack.....
d) Watch TV.....
e) Drink tea, coffee, cola .....
f) Drink water, soft drinks .....
g) Listen to music or radio.....
h) Take sleeping pills or tranquillizers .....
i) Shower or bath.....
j) Exercise or take short walks.....
k) Relaxation exercises (Meditation, Prayer).....
l) Engage in other activities .....

2 **How often does it take you more than 30 minutes to fall asleep?** .....

3 **How often are you unable to sleep at all?** .....

4 **Before falling asleep, how often do you experience any of the following:**
a) Coughing, breathing difficulties, suffocation.....
b) Feeling hot and sweaty.....
c) Headaches.....
d) Confusion/disorientation (do not know where you are) .....
e) Tension and worry .....

Scale: 0 = Never; 1 = Rarely; 2 = Sometimes; 3 = Often; 4 = Always; 5 = N/A

f) Unpleasant thoughts .....
g) Aches or pains in: limbs .....
neck.....
back.....
chest.....
abdomen.....
h) A need to move your legs because of unpleasant sensations in them.....
i) Sudden jerking movements of your arms and legs .....
j) Unable to move arms or legs.....
k) Unable to stop thinking about recent or past events .....
l) Frightening or strange hallucinations.....
m) Other (specify).....

5 **How often do you awaken more than 3 times at night?** .....

6 **If you awaken at night, how often do you stay awake more than 30 minutes before you go to sleep again?** .....

7 **If you awaken at night, how often do these awakenings happen during:**
a) the first third of the night.....
b) the second third of the night.....
c) the last third of the night .....

8 **How often are your awakenings during the night due to:**
a) External noises (telephone, baby crying noisy traffic) .....
b) Nightmares or unpleasant dreams.....
c) Aches and pains in different parts of the body (specify).....
d) Coughing, choking, breathing difficulties .....
e) Sudden jerking movements of arms and legs.....
f) Need to urinate .....
g) Heartburn .....
h) Headache.....
i) Other (specify).....

9 **During your sleep at night, how often have you noticed or have you been told that you do any of the following?**
a) Snore .....
b) Turn your head from side to side .....
c) Move your arms or legs or kick .....
d) Talk during your sleep .....
e) Walk during your sleep .....
f) Scream or shout.....
g) Grind your teeth.....
h) Cough.....
i) Suffer from interrupted breathing .....
j) Bed wetting .....

Scale: 0 = Never; 1 = Rarely; 2 = Sometimes; 3 = Often; 4 = Always; 5 = N/A

10 **How often is your sleep:**
a) Light
b) Deep

11 **How often do you have disturbing (bad) dreams during sleep?**

12 **When you wake up from these bad dreams, how often do you have the following?**
a) Feel relieved
b) Feel frightened
c) Have no emotion at all
d) Feel heart pounding
e) Breathe heavily
f) Choke
g) Feel pressure on your chest
h) Not able to move
i) Feel restless
j) Perspire
k) Scream
l) Wet your bed
m) Immediately fall asleep

13 **How often do you awaken in the morning feeling:**
a) Good mood
b) Bad mood
c) Refreshed
d) Physically tired
e) Headache
f) Muscle stiffness or pain in: limbs
neck
back
chest
abdomen

14 **How often do you nap during the day:**
a) On work/school days?
b) On weekends and holidays?

15 **How often do you feel refreshed after a daytime nap?**

16 **How often do you fall asleep during the following situations?**
a) While travelling (car, train, etc.)
b) In the movies or theatre
c) During talks or lectures
d) While watching TV
e) During social situations

Scale: 0 = Never; 1 = Rarely; 2 = Sometimes; 3 = Often; 4 = Always; 5 = N/A

f) While reading .....
g) During work .....
h) While driving a car .....
i) While eating .....
j) During other activities (specify) .....

17 **How often do you stop an activity because of an irresistible need to sleep?** .....

18 **During the day, how often do you:**
a) Feel refreshed and energetic .....
b) Feel physically exhausted and listless .....
c) Yawn .....
d) Have problems at work/school due to sleepiness or naps .....
e) Have attacks of sudden muscle weakness or falling .....
f) Have automatic activity (i.e., driving or walking without recalling where you are) .....
g) Feel faint or lose consciousness .....
h) Feel dizzy or unsteady .....
i) Have unusual sensation (numbness, tingling) in arms and legs .....
j) Have headaches .....
k) Have pain or discomfort in: limbs .....
neck .....
back .....
chest .....
abdomen .....

19 **How often do you have to work on shifts?** .....

20 **How often do you work on the:**
a) Day shift? .....
b) Evening shift? .....
c) Night shift? .....

21 **How often does your work require you:**
a) to stay awake most of the night? .....
b) to travel from one time zone to another? .....

22 **How often during your work are you exposed to:**
a) Continuous noises? .....
b) Monotonous activity? .....
c) Social isolation? .....
d) Pressures to increase your work output? .....

23 **How often have you used medications for the following purposes?**
a) to relieve pain (e.g. aspirin). Specify .....

b) to relieve heartburn or indigestion
(e.g. Antacids). Specify .....
c) to diminish nervousness (e.g. Tranquillizer)
Specify.....
d) to relieve depression (e.g. antidepressant)
Specify.....
e) to help you sleep better. Specify .....
f) to keep you awake during the day. Specify .....
g) caffeine tablets.....
h) against allergy (e.g. anithistamines). Specify .....
i) against asthma (e.g. aminophylline). Specify .....
j) to prevent convulsions (e.g. dilantin). Specify .....
k) to treat heart problems. Specify .....
l) to treat respiratory problems. Specify .....
m) to treat high blood pressure. Specify.....
n) hormones. Specify .....
o) to treat Parkinsonism. Specify .....
p) to reduce weight. Specify.....
q) other types of medicines. Specify .....
(1)
(2)
(3)

24 **How often have you used:**
a) Marijuana/hash?.....
b) Cocaine/crack? .....
c) L.S.D., mescaline, ecstasy? .....
d) Stimulants (speed drugs, uppers,
mood elevators, ephedrine)?.....
e) Narcotics (morphine, heroin, opium)?.....
f) Other. Specify?.....

SLEEP - WAKE QUESTIONNAIRE – Part II

INSTRUCTIONS

The following are statements that describe some measurable aspects of your experience.

Read each statement carefully and put in the appropriate box the nearest number that

describes your experience.

If the statement does not apply to you, put "N/A" on the appropriate line.

1. During work/school days, I usually sleep _____ hours.

2. During weekends and holidays, I usually sleep _____ hours.

3. If I nap, they usually last _____ minutes each .

4. During the past 6 months, I have had _____ nightmares each week.

5. During the past 3 years because of sleepiness : (a) I had _____ work accidents during day time.

(b) I had _____ work accidents during night time.
(c) I had _____ car accidents during day time.
(d) I had _____ car accidents during night time.

6. During the past month, I had to change: (a) from morning shift to night shift _____ times.
(b) from night shift to morning shift _____ times.
(c) from evening shift to night shift _____ times.
(d) from night shift to evening shift _____ times.
(e) from morning shift to evening shift _____ times.
(f) from evening shift to morning shift _____ times.

7. Each day I usually drink: _____ (a) cups of caffeinated coffee.
_____ (b) cups of regular tea
_____ (c) cups of herbal tea, Specify types: _____

8. Each day I usually take: _____ (a) vitamins; Specify _____
_____ (b) herbal remedies; Specify _____

9. Each day I usually smoke: _____ (a) cigarettes.
_____ (b) other; Specify _____

10. Each week I usually drink: _____ (a) glasses of cola.
_____ (b) glasses of wine.
_____ (c) bottles of beer.
_____ (d) ounces of liquor; Specify _____
_____ (e) ounces of other liquor; Specify _____

Scale: 0 = Never; 1 = Rarely; 2 = Sometimes; 3 = Often; 4 = Always; 5 = N/A

FAMILY SLEEP HISTORY

Please check (✓) in the proper space if any of the following items apply to a member of your family

		Son	Daughter	Brother	Sister	Father	Mother	Other (specify)
1	Sleep walking							
2	Screaming during sleep							
3	Very loud snoring in sleep							
4	Daytime sleepiness							
5	Other sleep problems (specify)							
	a)							
	b)							
6	Chronic fatigue							
7	Epilepsy							
8	Mental illness							
9	Psychiatric treatment							
10	Death during sleep							
	Chronic diseases:							
11	Cancer							
12	Heart diseases							
13	Rheumatoid arthritis							
14	Diabetes mellitus							
15	Other chronic disease							

Scale: 0 = Never; 1 = Rarely; 2 = Sometimes; 3 = Often; 4 = Always; 5 = N/A

HEALTH QUESTIONNAIRE

Please check (✓) in the proper space only the items in the following list that apply to you.

		During the Past Year A	More Than A Year Ago B
1	Diabetes		
2	Thyroid disorders		
3	Epilepsy		
4	Psychiatric illness		
5	Psychiatric treatment		
6	Neurologic disease		
7	Kidney disease		
8	Peptic ulcer, gastritis		
9	Intestinal disease (colitis)		
10	Liver disease		
11	High blood pressure		
12	Heart disease		
13	Headache		
14	Arthritis		
15	Back pain		
16	Obesity		
17	Asthma		
18	Pneumonia		
19	Enlarged tonsils, adenoids		
20	Repeated throat infections		
21	Chronic sinusitis		
22	Deviated Nasal Septum		
23	Other health problems (Specify)		
	Hospitalization:		
24	1 or 2 times		
25	3 or 4 times		
26	More than 4 times		
27	Surgery on mouth and/or nose (Specify)		

Scale: 0 = Never; 1 = Rarely; 2 = Sometimes; 3 = Often; 4 = Always; 5 = N/A

	For Women Only:		
28	Irregular menstrual periods		
29	Use of birth control pills		
30	Problems associated with menopause		

Brock University Sleep Research Laboratory
Sleep and Activity Diary

Study Start Date: _____

Name:
Date:

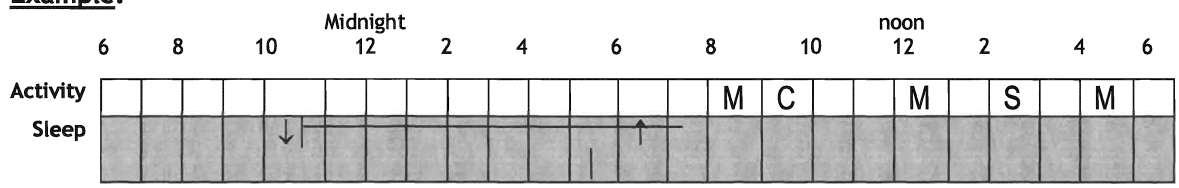
Instructions:

Sleep Log

- Leave the Sleep and Activity Diary by your bedside and complete each morning.
- An example of how the log should be marked is given at the bottom of this page.
- In the comments section of the each daily log, indicate anything unusual about the day (e.g., medications).
- The appropriate activities that should be logged include:

ACTIVITIES	
C	Any caffeinated drinks including coffee, tea, cola, etc.
A	Any alcoholic beverages
M	Meals
X	Exercise
T	Use of toilet during sleep time
S	Snacks
SLEEP (INCLUDING NAPS)	
↓	An arrow "down" roughly marks the time you went to bed
↑	An arrow "up" roughly marks the time you got out of bed
|	Mark with lines the time you began and ended your sleep
—	By joining these two lines you're indicating a sleep period

Example:



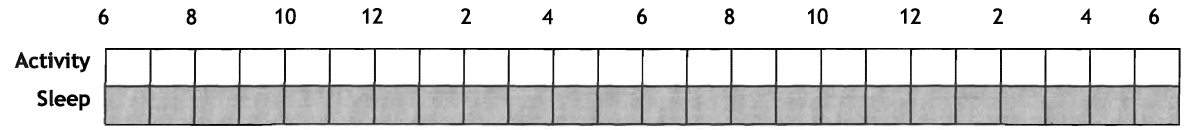
LIGHTS OUT ____10:30____ am/ [pm] TOTAL SLEEP DURATION ____7.45_____ hrs
Comments:_____Read for 15 minutes in bed before falling asleep_____

SLEEP LABORATORY CONTACT INFORMATION

Phone: 905-688-5550 ext 3795

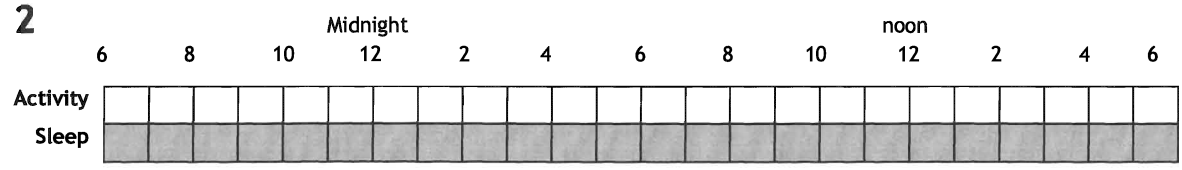
Email: cathmilner@gmail.com

Midnight noon



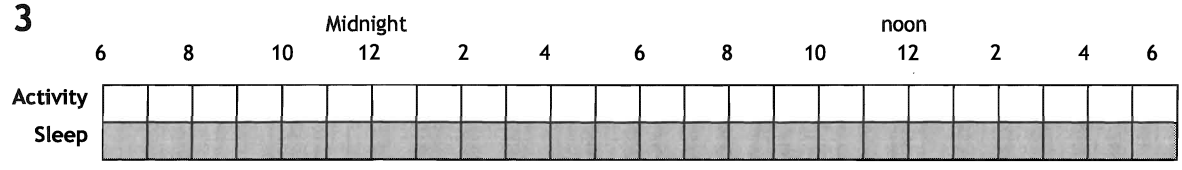
LIGHTS OUT _____ am/pm TOTAL SLEEP DURATION _____ hrs
Comments:_____

2



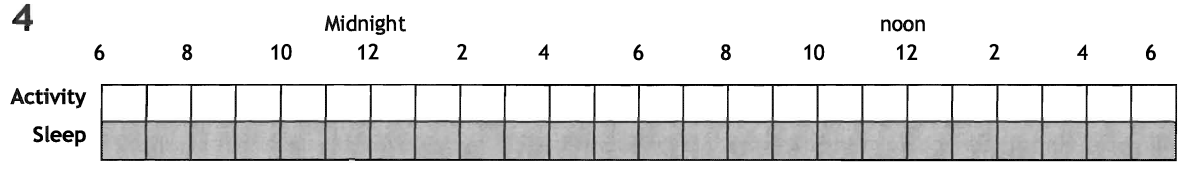
LIGHTS OUT _____ am/pm TOTAL SLEEP DURATION _____ hrs
Comments:_____

3



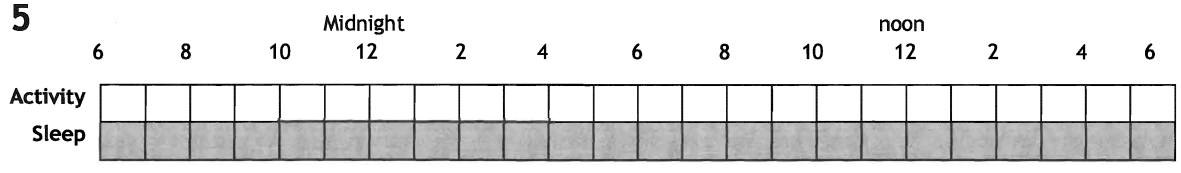
LIGHTS OUT _____ am/pm TOTAL SLEEP DURATION _____ hrs
Comments:_____

4



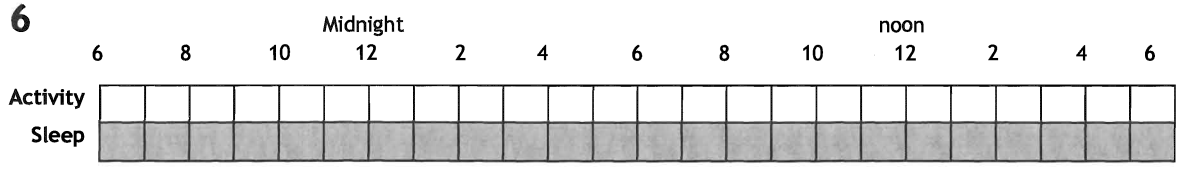
LIGHTS OUT _____ am/pm TOTAL SLEEP DURATION _____ hrs
Comments:_____

5



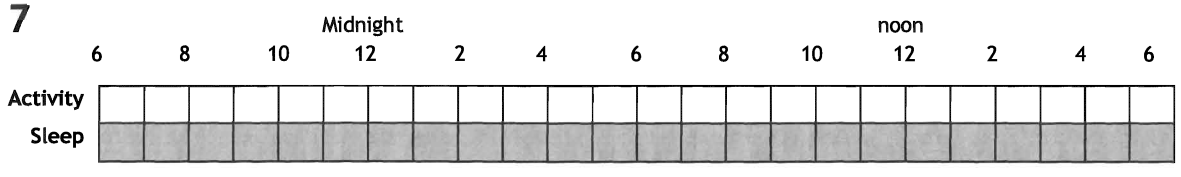
LIGHTS OUT _____ am/pm TOTAL SLEEP DURATION _____ hrs
Comments:_____

6



LIGHTS OUT _____ am/pm TOTAL SLEEP DURATION _____ hrs
Comments:_____

7



LIGHTS OUT _____ am/pm TOTAL SLEEP DURATION _____ hrs
Comments:_____

Pre-Sleep Questionnaire

Participant I.D. _____ Time:_____

Date: _____

At what time did you awaken today? _____a.m. p.m.

Has today been an unusual day in any way? No ___ Yes___. If yes, explain:

Did you fall asleep or take a nap today? No ___ Yes___. If yes, when and for how long:

Did you drink any alcohol today? No____ Yes____. If so, when _____
how much? _____

Did you, or will you, use any **medications** (prescription or non-prescription) **today?**
No____ Yes _____. If yes, **specify type and amount**:

Have you used any **prescription** medication in the **last 2 weeks**? No ____ Yes ____
If yes, **specify type and amount**:

Please indicate how many **cups or glasses** of the following that you have consumed today:

___ coffee, ___decaffeinated coffee, ___ tea, ___ cola, ____ chocolate drinks

At what time did you drink your **last** caffeinated beverage? _____a.m. p.m.

How long did it take you to fall asleep last night: _____ minutes

How much sleep do you think you got last night: _____hours

Please indicate with an **X** on the line:

|_____|

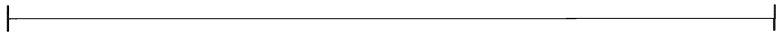
Best Possible Sleep **Worst Possible Sleep**

How many times do you think you woke up last night: _____ times.

Please mark each line with an 'X'

Going to bed

Asleep quickly — Long time awake



Felt very physically tense — Felt very physically relaxed

No worries on my mind — Many worries on my mind

Many thoughts — No thoughts

Felt very sleepy — Not exhausted at all

Had many physical ailments — Had no physical ailments

Went to bed in a very bad mood — Went to bed in a very good mood

During the night

Frequently awakened — Uninterrupted sleep

No noises — Very noisy

Very comfortable room temp. — Extremely hot or cold

Very comfortable bed — Very uncomfortable bed

Little or no body movement — Tossed and turned all night

Awakened and took and extremely long time to go back to sleep — Awakened but immediately went back to sleep

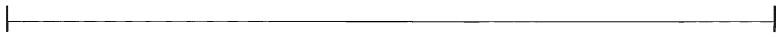
Lightest sleep possible — Deepest sleep possible

During the night (Continued)

Adequate amount of sleep — Not enough sleep at all

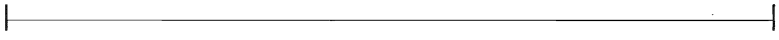
Many thoughts — No thoughts

Felt very physically relaxed — Felt very physically tense



Had many physical ailments — Had no physical ailments

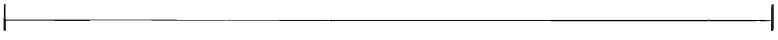
Extremely pleasant dreams — Extremely unpleasant dreams



Many dreams — No dreams

Upon awakening

Woke up long before or after I expected — Woke up exactly when I expected



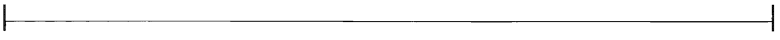
Woke up extremely tired — Woke up as rested as possible

Had a very hard time awakening — Woke up as easily as possible

Woke up in a very good mood — Woke up in a very bad mood

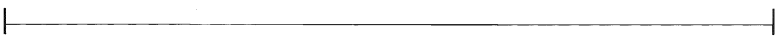
Remembered extremely unpleasant dreams — Remembered very pleasant dreams

Woke up feeling as physically poor as possible — Woke up feeling as physically good as possible



Woke up with no worries on my mind — Woke up with many worries

Woke up with no thoughts on my mind — Woke up with many thoughts



Put a check mark (✓) in the appropriate column to indicate if you are experiencing any of the following, **right now**.

	Not al All	Slightly	Moderately	Intensely
Headache				
Unsteadiness				
Faintness				
Breathing difficulties				
Chest pain				
Sweating				
Numbness [specify:]				
Flushing				
Chills				
Heart Palpitations				
Sexual feelings				
Hunger				
Bloating				
Nausea				
Gastric fullness				
Abdominal pain				
Feverishness				
Constipation				
Diarrhea				
Urinary problems				
Blurred vision				
Irritated eyes				
Puffy eyes				
Blacking out				
Noise in ears				
Reduced hearing				
Increased taste sensitivity				
Increased smell sensitivity				
Dry mouth				
Thirst				

Use the chart below to indicate the severity of any pains, aches, or stiffness that you may be experiencing right now.

On the chart a check (✓) in the row labelled '0' indicates no discomfort.
a check (✓)in the row labelled '6' indicates the worst possible discomfort.

	Head	Neck	Shoulders	Upper Limbs	Chest	Upper back	Lower Back	Abdomen	Hips	Lower Limbs
0										
1										
2										
3										
4										
5										
6										

Fatigue Scale

Please check (✓) the statement which best describes your present state of physical energy or fatigue.

	1	Full of energy: enough to tackle my usual physical activities.
	2	Energy level is quite high but not at its peak: most physical activities would pose no problem.
	3	Energy level is such that one would prefer to be doing very light or sedentary tasks at this point.
	4	Energy level is adequate for only routine activities at a leisurely pace.
	5	Energy level is such that it would be preferable to rest before doing any routine activity.
	6	Energy level is quite low: would strongly prefer to rest rather than do anything else.
	7	Totally physically exhausted: unable to undertake the least activity.

HOW DO YOU FEEL?

example: CALM ——X—— IRRITABLE

CALM |——————————————————————| IRRITABLE

HAPPY |——————————————————————| SAD

ENERGETIC |——————————————————————| SLUGGISH

RELAXED |——————————————————————| TENSE

STANFORD SLEEPINESS SCALE

Please check (✓) the statement which best describes your state of sleepiness. (Choose only **ONE** statement)

	1	Feeling active, vital, alert, or wide awake
	2	Functioning at high levels, but not at peak; able to concentrate
	3	Awake, but relaxed; responsive but not fully alert
	4	Somewhat foggy, let down
	5	Foggy; losing interesting in remaining awake; slowed down
	6	Sleepy, woozy, fighting sleep; prefer to lie down
	7	No longer fighting sleep, sleep onset soon; having dream-like thoughts

Post-Sleep Questionnaire

Participant I.D. _____ Time:_____

Date: _____

Please complete immediately upon the final awakening

How long did it take you to fall asleep last night: _____ minutes

How much sleep do you think you got last night: _____hours

Please indicate with an **X** on the line:

|---|

Best Possible Sleep **Worst Possible Sleep**

How many times do you think you woke up last night: _____ times.

How did last night differ from your usual night's sleep, taking into account that you slept in a different bed, with electrodes, etc.

Any comments or suggestions:

Please mark each line with an 'X'

Going to bed

Asleep quickly — Long time awake

Felt very physically tense — Felt very physically relaxed

No worries on my mind — Many worries on my mind

Many thoughts — No thoughts

Felt very sleepy — Not exhausted at all

Had many physical ailments — Had no physical ailments

Went to bed in a very bad mood — Went to bed in a very good mood

During the night

Frequently awakened — Uninterrupted sleep

No noises — Very noisy

Very comfortable room temp. — Extremely hot or cold

Very comfortable bed — Very uncomfortable bed

Little or no body movement — Tossed and turned all night

Awakened and took and extremely long time to go back to sleep — Awakened but immediately went back to sleep

Lightest sleep possible — Deepest sleep possible

During the night (Continued)

Many thoughts — No thoughts

Felt very physically relaxed — Felt very physically tense

Had many physical ailments — Had no physical ailments

Extremely pleasant dreams — Extremely unpleasant dreams

Many dreams — No dreams

Upon awakening

Woke up long before or after I expected — Woke up exactly when I expected

Woke up extremely tired — Woke up as rested as possible

Had a very hard time awakening — Woke up as easily as possible

Woke up in a very good mood — Woke up in a very bad mood

Remembered extremely unpleasant dreams — Remembered very pleasant dreams

Woke up feeling as physically poor as possible — Woke up feeling as physically good as possible

Woke up with no worries on my mind — Woke up with many worries

Woke up with no thoughts — Woke up with many thoughts on my mind

Put a check mark (✓) in the appropriate column to indicate if you are experiencing any of the following, **right now**.

	Not al All	Slightly	Moderately	Intensely
Headache				
Unsteadiness				
Faintness				
Breathing difficulties				
Chest pain				
Sweating				
Numbness [specify:]				
Flushing				
Chills				
Heart Palpitations				
Sexual feelings				
Hunger				
Bloating				
Nausea				
Gastric fullness				
Abdominal pain				
Feverishness				
Constipation				
Diarrhea				
Urinary problems				
Blurred vision				
Irritated eyes				
Puffy eyes				
Blacking out				
Noise in ears				
Reduced hearing				
Increased taste sensitivity				
Increased smell sensitivity				
Dry mouth				
Thirst				

Use the chart below to indicate the severity of any pains, aches, or stiffness that you may be experiencing right now.

On the chart a check (✓) in the row labelled '0' indicates no discomfort.
a check (✓)in the row labelled '6' indicates the worst possible discomfort.

	Head	Neck	Shoulders	Upper Limbs	Chest	Upper back	Lower Back	Abdomen	Hips	Lower Limbs
0										
1										
2										
3										
4										
5										
6										

Fatigue Scale

Please check (✓) the statement which best describes your present state of physical energy or fatigue.

	1	Full of energy: enough to tackle my usual physical activities.
	2	Energy level is quite high but not at its peak: most physical activities would pose no problem.
	3	Energy level is such that one would prefer to be doing very light or sedentary tasks at this point.
	4	Energy level is adequate for only routine activities at a leisurely pace.
	5	Energy level is such that it would be preferable to rest before doing any routine activity.
	6	Energy level is quite low: would strongly prefer to rest rather than do anything else.
	7	Totally physically exhausted: unable to undertake the least activity.

HOW DO YOU FEEL?

example: CALM ——X—— IRRITABLE

CALM |——————————————————————| IRRITABLE

HAPPY |——————————————————————| SAD

ENERGETIC |——————————————————————| SLUGGISH

RELAXED |——————————————————————| TENSE

STANFORD SLEEPINESS SCALE

Please check (✓) the statement which best describes your state of sleepiness. (Choose only **ONE** statement)

	1	Feeling active, vital, alert, or wide awake
	2	Functioning at high levels, but not at peak; able to concentrate
	3	Awake, but relaxed; responsive but not fully alert
	4	Somewhat foggy, let down
	5	Foggy; losing interesting in remaining awake; slowed down
	6	Sleepy, woozy, fighting sleep; prefer to lie down
	7	No longer fighting sleep, sleep onset soon; having dream-like thoughts

Average Number of Trials in Grand Averages

	Control Group			TBI Group		
Evoked KCs	*Target*			*Target*		
Stage 2	100			71		
Paired-Click	*Stimulus 1*	*Stimulus 2*		*Stimulus 1*	*Stimulus 2*	
Pre-Sleep Wake	50	49		44	44	
Post-Sleep Wake	47	47		41	40	
Stage 2	389	397		374	391	
REM	250	250		232	235	
Oddball	*Standard*	*Target*		*Standard*	*Target*	
Pre-Sleep Wake	268	65		251	60	
Post-Sleep Wake	252	60		230	56	
Early Stage 2	1132	194		1005	180	
Late Stage 2	1457	330		1544	344	
SWS	1130	258		1192	270	
REM	1012	265		930	233	
N-back	*Standard*	*Target*		*Standard*	*Target*	
Pre-Sleep Night 1	114	42		110	42	
Post-Sleep Night 1	111	43		99	39	
Pre-Sleep Night 2	119	43		109	43	
Post-Sleep Night 2	114	44		97	38	
Novel P3	*Standard*	*Target*	*Novel*	*Standard*	*Target*	*Novel*
Pre-Sleep Night 1	183	22	22	167	20	20
Post-Sleep Night 1	173	20	21	156	19	18
Pre-Sleep Night 2	189	23	22	168	21	20
Post-Sleep Night 2	172	19	21	156	20	19
Visual RT	*Errors*			*Errors*		
Waking Average	74			52		